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ON THE SURGICAL IMPORTANCE OF THE VISCERAL CRISES IN THE ERYTHEMA GROUP OF SKIN DISEASES.

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The possibility of mistaking these visceral crises for appendicitis or intussusception or obstruction of the bowel, and handing the patient over to the surgeon for operation, is by no means remote. In Case II. of my series[1] one attack was unilateral, and of such severity that the physician who was called in, knowing nothing of the previous history of the case, diagnosed renal colic. In Case XX. the child was admitted to the surgical wards supposed to have appendicitis. Fortunately the skin rash was noticed, the pain subsided, and he was transferred to the medical wards. The association of the colic with the passage of blood *per rectum* may, of course, lead to the diagnosis of intussusception. In the January number of the *British Journal of Children's Diseases*, vol. i., No. 1, Dr. G. A. Sutherland reports the case of a boy, aged five years, who, eight days before admission, had been seized with severe abdominal pain and vomiting. After continuing intermittently for four days the attack passed off, but recurred two days later in a more persistent manner. The day before admission the motions were blood-stained. The boy looked very ill; the abdomen was distended, and he had recurring attacks of severe colic. The temperature was normal. The next day the abdomen was more distended and palpation was impossible. It was decided that the symptoms indicated obstruction from intussusception. The abdomen was

[1] The American Journal of the Medical Sciences, January, 1904.

opened and the sigmoid flexure was found much distended; "on going over the small intestine a part of the bowel about five inches long was found, which was dark in color, evidently from extravasated blood, and with thickened walls." There were no other hemorrhages visible. The boy reacted well from the operation, and for the next five days he had only occasional pains. He then for the first time had a skin eruption, with albumin in the urine, and the diagnosis was cleared up.

In a second case reported by Dr. Sutherland, a girl, aged seven years, was admitted to hospital with Henoch's purpura. She had a prolonged illness with the usual attacks of abdominal pain, vomiting of blood, melæna, albuminuria, and hæmaturia. She gradually recovered, and three months later was readmitted with a recurrence of all the symptoms. The pain was more severe, referred to the umbilicus, spasmodic and colicky in character. There were hemorrhages similar to the previous attack. She died in a general convulsive seizure. The temperature was 104° F. There was acute general peritonitis and intussusception of the cæcum and part of the ileum into the colon. The involved portions of the intestine were black and hemorrhagic and gangrenous. As Dr. Sutherland rightly surmises, the fatal attack was induced by hemorrhage into the wall of the colon, leading to paralysis of the affected part and to increased muscular contraction, with colic, in the adjoining part of the bowel. As a result of these strong muscular contractions the sound part of the intestine became invaginated into the paralyzed and hemorrhagic portion.

In the same journal there is reported by Mr. Harold Burrows a case in which laparotomy was performed. A boy, aged eleven years, was admitted to the Bolingbroke Hospital July 6th with a diagnosis of obstruction from intussusception. After feeling out-of-sorts for ten days, on the morning of the sixth he was seized with violent pain in the abdomen and vomiting, and shortly afterward passed blood, the vomitus being dark brown, with a fecal odor. There was general tenderness of the abdomen; no distention; no lump. The abdominal muscles were held rigid. The patient was examined under an anæsthetic, and it was decided to operate. A few inches from the ileocæcal valve the ileum showed small petechial hemorrhages and some irregular patches of congestion. The peritoneum over these parts was sticky and had lost its gloss. On the following day the patient was free from pain, but it was then noticed that there was a skin eruption. From the history the boy had had on June 26th, eleven days before admission, some arthritis and a skin rash.

The following case, at present in my wards, is a further illustration of the surgical importance of this group of cases.

Lena F., aged seventeen years, admitted for the first time December 1, 1903. The patient was seen by Dr. McCrae in consultation

with her attending physician. She was in bed, rolling about with the pain, and at times assumed very curious positions, getting in the knee-elbow position and crouching and bending, very rarely staying very long in any one place. The pain was evidently of great severity, paroxysmal in character. Examination of the abdomen was negative. There was no tenderness anywhere on pressure; no resistance. The knee-joints were slightly swollen and quite tender. There was no skin eruption; no fever. She had had large doses of morphine hypodermically, which only relieved the pain for a short time. The association of the arthritis made Dr. McCrae suspicious of the form of abdominal colic associated with skin lesions and nephritis. She was removed to the hospital with some difficulty.

The history obtained was as follows:

She had been a healthy girl. The family history was excellent except that the mother was very neurotic. There was no rheumatism in the family. She had been very well as a child and had grown and thriven. Six months before admission she had her first attack of pain in the abdomen, which every week or two had recurred and had been very severe. The attack was usually associated with vomiting. It had no relation to food, never associated with jaundice; no chills. The bowels were obstinately constipated. The attacks recurred with great severity, and on August 3d an exploratory operation was made at the City Hospital—an incision in the upper part of the abdomen. The gall-bladder was found to be clear and there was no sign of gastric ulcer; no appendicitis. Three weeks after the operation the attacks recurred, and she has had a number of very severe paroxysms. On admission she was a healthy-looking, well-nourished girl. The abdomen was not distended; no special tension; palpation could be made readily in all regions and was negative. Examination of the thoracic organs was negative. The knee-joints were a little swollen and tender, not red. Examination of the gastric juice on two occasions showed nothing special. The stools were searched carefully without finding anything abnormal. For the first few days after admission she had attacks of pain lasting from one and a half to two minutes, colic-like in character, readily controlled with codeine. She vomited on December 1st. There was no special change in the leukocytes. The count on admission was normal; coagulation time three minutes. On December 5th she had slight bleeding from the nose. On the 6th there was a trace of albumin in the urine, which persisted, and toward the close of her stay in the hospital there were a few hyaline casts. There was no skin rash. The knee condition rapidly disappeared. She was discharged December 15th, very much improved.

She was readmitted January 28, 1904. She had been very much better, but she had had slight attacks. On January 25th the colic became very severe and she had much nausea. She had had

recurring attacks of bleeding from the nose, and once, she said, bleeding from the gums. There had been no skin eruption. The knee-joints became swollen and painful shortly after admission. The leukocytes were 12,500. The urine on the 29th (catheterized specimen) was smoky, and contained albumin in small amount, a few red corpuscles, and numerous hyaline casts. She remained in the hospital for nine days; the pains lessened, and she improved in her general condition.

The practical lessons to be drawn from these three cases in which laparotomy was performed are: first, that in children with colic the greatest care should be taken to get a full history, which may bring out the fact of previous attacks, either of skin lesions, of arthritis, or of intestinal crises; and secondly, to make the most careful inspection of the skin for angioneurotic œdema, purpura, or erythema. It is also to be borne in mind that recurring colic may be for many years the sole feature of this remarkable disease, as in Cases XVII. and XXVII. of my series, in which the obscurity of the attacks of colic was not cleared up until the final appearance of skin lesions. In the case here reported the intestinal crises, in combination with arthritis and the renal features, leave no doubt as to the diagnosis. In her next attack there may be purpura or angioneurotic œdema, or an acute nephritis may occur alone. The colic is the most constant of the visceral manifestations, occurring in twenty-five of the twenty-nine cases in my series. So far as I know, it is never dangerous. In no case recorded has death resulted, I believe, from intestinal causes. The examination in the cases of Dr. Sutherland and Mr. Barrows confirms the view that the colic is due to infiltration of the intestinal wall with blood and serum.

CHANGES IN THE INTERCOSTAL MUSCLES AND THE DIAPHRAGM IN INFECTIVE PROCESSES INVOLVING THE LUNG AND PLEURA.[1]

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So far as the writer is aware, no important study has been undertaken of the relation, if any, existing between the intercostal muscles and inflammations of the lung and pleura, or of either alone. An examination of the most important text-books on medicine and pathology discloses no reference to characteristic anatomical changes in the intercostal muscles or nerves in any of the conditions under consideration.

[1] Read before the Pathological Society of Philadelphia, January 28, 1904.

Aufrecht,[1] in a most exhaustive article on pneumonia, notes the occurrence of severe intercostal pain and pain in the abdominal muscles, both of which are attributed to the cough, and this seems to be the view held by other observers. It is reasonable to assume that the cough induces muscular soreness, comparable to the soreness resulting from any other form of muscle fatigue, but, in some cases at least, muscle pain and tenderness may depend upon demonstrable lesions in the affected tissues.

Rosenbach,[2] in his elaborate article on pleurisy, speaks of atrophy of the thoracic muscles and antagonistic muscles, and briefly refers[3] to the fact that changes occur in the costal pleura and intercostal muscles during perforation.

Again,[4] without any special detail as to the character of the lesions, he refers to degeneration of the thoracic muscles in acute and chronic pleurisies. The same writer notes that certain of the sensations apparently arising in the intercostal spaces resemble muscle pain,[5] and that in large exudations where muscles and pleura are "much involved," the intercostal depressions are obliterated, so as to admit of deep pressure. He does not refer to these phenomena as indicating a period of relaxation in the muscle, although that seems to be the probable explanation.

In an editorial note Musser refers to a case in which pleurisy and intercostal neuralgia were concurrent. In the first week signs of pleurisy dominated; in the second, third, and fourth weeks intercostal neuralgia was most evident. An herpetic eruption developed along the course of the ninth intercostal nerve.

Rosenbach[6] refers to marked dyspnœa if there be much pain in the thoracic muscles, and speaks of rheumatic pains in these muscles as accompanying dry pleurisy. In common with other observers, he[7] notes the respiratory asynchronism evinced by delayed excursion on the affected side. The chest deformity associated with contracting thorax, he says, may be due to degenerated and contracted muscles[8] and the intercostal spaces may be obliterated, the ribs overlying each other like tiles on a roof.

The same writer[9] is of the opinion that in affections of the thoracic muscles, such as rheumatism and intercostal neuralgia, contraction of the intercostal muscles may give rise to conditions that simulate dulness; at just this point it might be well to note that œdema, perivascular infiltration, and lipomatous change of the intercostal muscles would, theoretically, favor the same result. With full recognition of his entire unfittedness, it is not the writer's purpose to discuss the influence of the alteration in the intercostal tissues on physical signs, but any of the mentioned changes in the intercostal

[1] Diseases of the Bronchi, Lungs, and Pleura, Nothnagel's Encyclopedia, 1903, p. 455.
[2] Ibid., p. 826. [3] Ibid., p. 830. [4] Ibid., p. 882. [5] Ibid., p. 845.
[6] Ibid., p. 849. [7] Ibid., p. 852. [8] Ibid., p. 853. [9] Ibid., p. 856.

muscles would presumably influence the percussion note and probably modify the auscultatory sounds.

With regard to the pseudopleural friction sound, called by the French *bruit de cuir neuf*, Rosenbach[1] accepts the condition as a muscle phenomenon, and it is not improbable that other pseudopleural friction sounds are, at least in part, of muscle origin. As will be shown later, pleurisy may be complicated with a myositis, and it would be of great interest to know if any friction sound results from movement in muscles the seat of inflammation. This could be determined, probably with great accuracy, by auscultation of muscles so situated as to exclude the probability of friction sounds arising from any other cause. It is well known that œdema of collagenous membranes, such as tendon sheaths, may give rise to friction sounds, and it is not impossible that the septal fibres or septal membrane between the external and internal intercostals, and possibly the movement of fibre sheaths or bundles, one upon another, might give rise to such friction.

Przewalski[2] calls attention to the narrowing of the intercostal spaces and increased resistance to intercostal digital pressure in all of 19 cases of pleurisy, 14 of which were serous and 5 suppurative. The sign is most easily elicited in children. He regards this narrowing of the intercostal spaces and fixation of the intercostal muscles as characteristic of pleurisy and analogous to *les attitudes fixes des membres* in inflammations of the joints. He does not seem to have suggested that the phenomenon he observed could have depended upon architectural change in the muscles of the area to which he draws special attention.

Although Rosenbach[3] speaks of extension by contiguity from pleura to peritoneum, the anatomical changes in the diaphragm accompanying such extension received no specific notice. The only study of the muscles of respiration in pneumonia and pleurisy with which I am familiar is that by Rohrer.[4] This observer made a careful study of the diaphragm in pneumonia, pleurisy, and pericarditis, and shows that in pneumonia and pleurisy an interstitial myositis of the muscular portion of the diaphragm adjacent to the area involved, whether it be pleura, pericardium, or peritoneum, frequently results. His studies include only lesions of the muscle areas of the diaphragm; he makes no reference to any involvement of the tendon. His excellent paper is illustrated by a number of exceptionally good photomicrographs of the condition that he describes. This phrenitis or diaphragmitis, Rohrer believes, may result from (1) direct extension, (2) extension by the lymphatics, and (3), though rarely, hæmatogenous infection.

[1] Diseases of the Bronchi, Lungs, and Pleura, Nothnagel's Encyclopedia, 1903, p. 864.
[2] Centralbl. f. Chir., 1902, vol. xxix. p. 377. [3] Ibid., p. 830.
[4] Maryland Medical Journal, September, 1902, No. 9, vol. lxv. p. 391.

PERSONAL OBSERVATIONS. The writer has studied the intercostal muscles in 7 cases; 2 of these were croupous pneumonias with plastic pleurisies, the pneumococcus being isolated from the lung and pleural effusion. Two were tuberculous lesions of the pleura; one of them a direct extension of tuberculosis to the pleura from a large area of recent tuberculous pneumonia in the presence of a dense fibrous adhesion, irregular in outline, 12 cm. in length anteroposteriorly, and possessing a maximum breadth of 6 cm., situated immediately over and involving the lower portion of the upper lobe of the right lung; the anterior margin of the sclerotic area corresponding to the costocartilaginous junction. The other case was a frank tuberculous serofibrinous pleurisy, acute in time, the tubercle bacillus being demonstrable in films from the exudate, and the condition associated with a number of chronic tuberculous lesions of the lung, some of which were fibroid, partly encapsulated, others evidently more recent. Two other cases were acute pneumococcal pleurisies, one in a child (seven years), the other in an adult, and associated with pericarditis. The seventh case was a chronic empyema, for which Professor Keen performed an extensive resection of the thoracic wall.

In both cases of croupous pneumonia the diaphragm was also examined. One case showed the acute leukocytic infiltration similar to that described by Rohrer, with, at points, evident beginning abscess formation. This is evinced by areas of necrosis extending the breadth of six to eight muscle fibres, the necrotic detritus being richly infiltrated with polymorphonuclear and hyaline leukocytes. At such points, by appropriate staining methods, organisms possessing the morphology and tinctorial characters of the pneumococcus can readily be demonstrated. The change not mentioned by Rohrer, but clearly made out in this case, is an evident involvement of the lymphatic tracts of the tendon of the diaphragm. Sections of this tissue show irregular columns of leukocytes arranged parallel with the fibres and sometimes so solidly grouped as to constitute almost an injection of what appears to be a lymph vessel. Within the muscle area and occasionally in the tendon the fibrin content of the exudate can be demonstrated satisfactorily by Weigert's fibrin stain.

Fragmentation of the muscle fibres and the appearance within them of phagocytic leukocytes would indicate that an attempt was being made to clear up the areas of necrosis by the ordinary process for the removal of necrotic tissue. In this particular instance I have found no evidence of further effort at repair. The acuteness of the process probably explains this finding. The change in the muscle, so far as can be determined from the examination of a single specimen, is restricted to the side involved. In the tendon, however, the lesion is a little more diffuse. The diaphragm in the other case of pneumonia and also the intercostal muscles in the same case show practically no structural alteration, at least nothing that could not be

attributed to such variation in spacing of fibres and in size as might be found in any muscle. The changes found in the other 5 cases may be grouped together with the case of acute tuberculous pleurisy. They were not marked. In another case the lesion is much more advanced, and later will be described in detail. In the two acute pneumococcal infections engrafted on catarrhal pneumonia, the lesions are evident and clearly recent; the one chronic case must be considered separately.

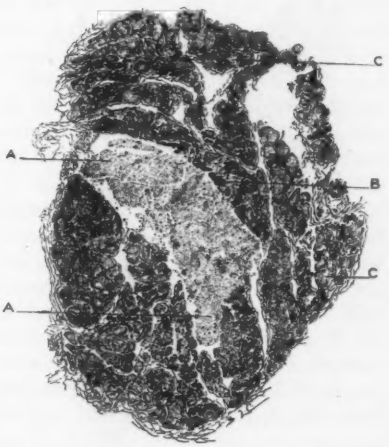
The number of cases examined is, of course, too small to determine with accuracy, and, to the satisfaction of the critical observer, the exact order in which the lesions occur. Probably the following order will require revision upon more extended observation; it is at present submitted more for the purpose of indicating the character of the lesions found than with the idea of definitely establishing the chronological order in which the processes occur:

1. Muscle fibres showing marked granular change, inadequate tingibility, and unsatisfactory stain reaction, such as commonly observed in granular tissues, can be recognized in all cases. It is not clear that this granular degeneration or cloudy swelling can be attributed to inflammation in the adjacent serosa, as it closely resembles, indeed, is probably identical with, the cloudy swelling observed in muscles as a result of infectious processes where apparently the toxin is acting through the blood. It would, therefore, seem wise to regard this change as a part of an alteration affecting the general musculature, the intercostals, in common with other muscles, manifesting their share in the change induced by the systemic action of toxic bodies.

2. With this alteration probably begin the changes that are incident to the involvement of and extension from the adjacent serosa. Muscle fibres are dissociated, the separation in some instances being quite distinct. The presence of a granular acidophilic deposit around the muscles and interfascicular connective tissue indicates that we are dealing with an œdema; but few leukocytes can be seen in this stage. The muscle cells stain poorly; the connective tissue does not respond with its wonted activity to the usual connective-tissue dyes. The component cells are swollen and granular, and occasionally a faint network of fibrin can be demonstrated at selected points. There is not, however, in this stage, any conspicuous addition of a fibrin-containing substance. With this condition, bands, groups, and bundles of muscle fibres may be seen showing a change that, so far as I can observe, cannot be differentiated from the hyaline, vitreous, or diaphanous degeneration described by Zenker, known to occur in the muscles of the abdominal wall in typhoid, and now recognized to be a much more widely distributed lesion often found in other conditions. In these hyaline areas muscle fibres often appear to coalesce, so that the hyaline change seems to include the interfascicular tissue as well as the

muscle fibre. Whether this change be a secondary degeneration or necrosis, probably our present methods are inadequate to determine. That it is not identical with coagulation necrosis containing fibrin can easily be established by the absence of fibrin in some areas where the process now under consideration is conspicuous; we are familiar with processes clearly necrotic and closely resembling, if not identical with, the change now under consideration, that could not, with propriety, be grouped with the necroses. As this, however, is neither the time nor the place to enter into the academic discussion as to what constitutes necrosis and what degeneration, it does not seem necessary to consider further the change present, the appearance of which is fairly well reproduced in Fig. 1.

FIG. 1.

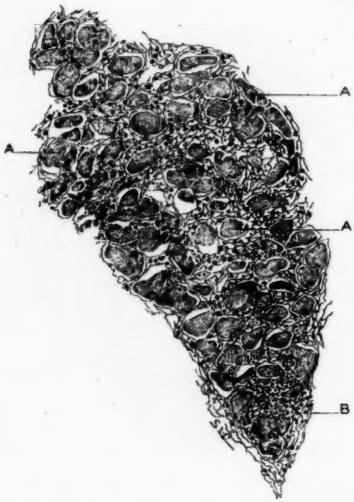


Intercostal muscle, transverse section, from a case of epipneumonic pleurisy, showing area of necrosis. Tissue fixed in Zenker's fluid; hæmatoxylin and eosin stain. A, A. Necrotic area in some portions of which the shadowy outlines of muscle fibres may still be distinguished, B. A few mononuclear leukocytes, mostly of the lymphoid type, aggregated on the margin of the necrotic area. C, C. Fragmenting vacuolated fibres, of which several can be seen in the field.

3. It seems reasonable to assume that the stage now to be described is preceded, at least in some instances, by the alterations mentioned above. The dissociation of the fibres, the granular material, the areas of hyaline change, can still be recognized, or at least appearances of their having been present may be more or less fully identified. In this stage there is a leukocytic infiltration of the muscle similar to that shown in the photographs illustrating Rohrer's article. The leukocytes present in the specimen studied are mostly of the mononuclear type, many of them corresponding to the large lymphocyte or hyaline cell; the polymorphonuclears have not been exceedingly numerous; eosinophiles have not been identified in the altered areas. The dissociation, fragmentation, granularity, and necrosis of the muscle fibres are in this stage very much more evident. It is a diffuse process; some of the fibres appear to suffer

to a marked degree, almost amounting to a necrosis, while others but slightly altered may be seen immediately adjacent, in a way resembling very closely the myocardial degenerations that have been described in various infectious diseases. (See Fig. 2.) Fibrin is abundantly present; bacteria may be conspicuous, while in the preceding forms they were at most but scanty and usually absent. There is in this stage no difficulty in the identification of organisms that in the pneumonias and epipneumonic pleurisies may, with reasonable certainty, be considered pneumococci. Sometimes the bacteria are grouped in the spaces between the muscle fibres in such a manner as to indicate dissemination along a lymph vessel, possibly only a larger lymph space.

FIG. 2.



Intercostal muscle, transverse section, from a case of epipneumonic pleurisy, showing dissociation of fibres, interfascicular leukocytic infiltration, and slight fibrin formation. Tissue fixed in Zenker's fluid; hæmatoxylin and eosin stain. A, A, A. Granular and fragmented muscle fibres. B. Accumulation of leukocytes and fibrin around and extending between the muscle fibres. In some areas the change is more marked than in others, and at points many polymorphonuclear leukocytes can be seen.

It has not been possible to secure specimens showing what might be looked upon as the next stage, and as to the ultimate outcome, should the patient recover, it is not possible at the present time to offer any unassailable opinion. Evidence of abscess formation is usually absent; the process seems more diffuse, but one could easily appreciate that the small necrotic areas infiltrated by polymorphonuclear leukocytes are really microscopic abscesses, such as can readily be demonstrated in the diaphragm. Our knowledge of the pathology of muscle inflammations leads us to infer that with the subsidence of active infection the necrotic muscle fibres would be removed by phagocytic cells (myoclasts); the interfascicular exudate would undergo absorption, and, with the formation of a certain amount of fibrous tissue, there would eventually result a moderate

degree of muscle sclerosis. It therefore seems reasonable to assume that where the disease lasts a sufficient length of time—where, in other words, the infection is permitted to continue—the changes between the stages just described and the conditions found in the specimen examined and reported below would fall under the head of subacute or chronic sclerosing myositis, which, toward the end, would give rise to the picture presented in the following case.

For the privilege of reporting this case I am under particular obligation to Professor Keen, who kindly placed at my disposal his notes and description of the operation, from which I summarize as follows:[1]

F. A., male, aged twenty-two years. Admitted to the Jefferson Hospital on June 11, 1903. Patient of Dr. Boyer.

Left-sided pleurisy of six years' duration, terminating in empyema. Upon admission to the hospital the left side of the chest was fuller than the right. The intercostal spaces obliterated. Mediastinal organs displaced to the right. June 9, 1903, aspiration; three quarts of yellowish pus withdrawn. On June 16th Dr. Stewart excised two inches of the seventh rib on the left side at the anterior axillary line, opened the pleural cavity, evacuated a large quantity of greenish-yellow, turbid fluid, and inserted two drains. Bacteriological examination by Dr. Rosenberger at this time showed cultures of the micrococcus pyogenes aureus and albus. The urine contained albumin, hyaline and granular casts. Under drainage the patient improved and left the hospital on June 28th. Daily irrigation of the cavity was practised for some time before leaving the hospital. He was readmitted under Professor Keen's care on October 26th. The heart was still displaced somewhat to the right; the left side of the chest was still flat; diminished resonance over left lung, with respiratory sounds diminished in upper and absent in lower half of organ. Urine contained trace of albumin, but casts were not detected. Tubercle bacilli were not found in the discharge from the pleura. Pneumococci noted as absent. Staphylococcus pyogenes aureus still present, and an organism possessing the morphology and tinctorial characters of the diphtheria bacillus, but without pathogenic action for animals, was obtained in studies made by Dr. Rosenberger.

On November 4th Professor Keen again submitted the patient to operation, and the following record is from his notes:

"I made the usual large flap extending from the second rib, with a broad sweep under the arm down to the level of the seventh rib, and backward between the scapula and the spine. The entire thickness of the chest-wall, including a greatly thickened pleura, was then removed from the third to the seventh ribs, inclusive. The pericardium and pleura were exposed. I made no attempt at decor-

[1] The physical signs were characteristic and need not be detailed.

tication, but only curetted the parts thoroughly, because the patient's condition was bad, with his heart pushing over to the right side, the left lung of very little use, and the right hampered by the displacement of the heart and the left lung; the operation was finished as rapidly as possible; after replacing the flap, which left a large opening at the lower portion, and packing some iodoform gauze to check the slight oozing, the wound was closed.

"On December 2d there were evidences of a beginning œdema of the lungs; he rapidly failed and died on the 4th."

No autopsy was obtained.

The specimen removed came to the laboratory for study and was submitted for examination to Dr. Ellis, Demonstrator of Morbid Histology, whose report is as follows:

"The specimen consists of a number of pieces of ribs varying from 2 cm. to 9 cm. in length, to which are attached masses of tissue; portions of this tissue are grayish in color, dense, and apparently fibrous. The surface of some of the masses is yellowish or yellowish-gray and shows areas of necrosis. Small fragments of muscle are also attached.

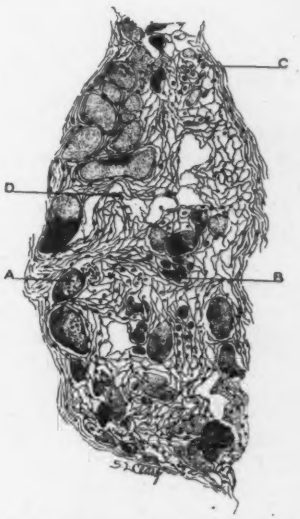
"The soft parts were fixed in Bensley's fluid, dehydrated, cleared, and infiltrated with paraffin. Sections were cut and stained by the usual laboratory methods.

"Microscopic examination shows the majority of the sections to be made up of fibrous tissue, most of which is in the early stages, though certain parts are quite dense. The margin of the sections bordering the most recent fibrous tissue is composed of embryonic and granulation tissues in which are numerous polymorphonuclear leukocytes. Beneath this formative zone is fibrous tissue in various stages of formation. Some of the sections contain considerable striated muscle, which has undergone pronounced changes. Certain areas show a high degree of fatty infiltration, while in others this is associated with a marked increase of the fibrous tissue. The latter change is for the most part fairly recent in point of time. The muscle fibres show varying degrees of atrophy. Vacuolization and fragmentation of the fibres are also seen."

It will be observed that this specimen shows marked atrophy and advanced destruction of the muscle fibres, with intercalation of newly formed and forming fibrous tissue with, at points, advanced substitutive lipomatous infiltration. It seems reasonable to assume that the long-continued infection of the pleura has given rise to this alteration in the intercostal muscles. These structures in this specimen show no evidence of an existing infection. The process has assumed a very much more chronic type manifested by the development of formative tissue in the intramuscular septa and in the interfascicular spaces. Necrotic processes are no longer active in the muscles. Fig. 3 represents a small area from this specimen, and shows to advantage the essential changes in the muscular tissue.

PATHOGENESIS. It seems to the writer that the cause of these changes in the intercostal muscles is clear. Feiner has shown that after injecting fluids containing suspended granules into the pleura the extraneous matter may be demonstrated in the costal pleural lymphatics, and that but little resorption takes place through the pulmonary pleura. When we consider the fact that in inflammations of the lung and pleura the interlobular and intralobular lymphatic systems can be seen engorged with products of absorption from the lung principally, we can understand how the parietal or costal lymphatic system must necessarily care for the major part of the drainage from the pleural cavity. This being the case, toxic materials passing off by this route are brought in close proximity to the inter-

FIG. 3.



Intercostal muscle, transverse section, from a case of suppurative pleurisy of several months duration, showing advanced fibrosis and lipomatous change. Tissue fixed in Zenker's fluid; hæmatoxylin and eosin stain. A. One of several granular fibres, some of which are fragmented and undergoing absorption. B. A small group of greatly shrunken muscle fibres. C Relatively large mononuclear cell, not very abundant but commonly associated with fibroblastic elements. D. The leader from this letter passes between two imperfectly preserved fat bodies, a number of which are present in the newly forming or formed fibrous tissue. The fat content is scanty in the particular field from which this drawing is made.

costal muscles and diaphragm; it seems reasonable to assume that direct lymphatic paths may become occluded, being in close proximity to the centres of irritation, and, therefore, collateral currents must form through the intercostal muscles, thereby exposing them to the dangers induced by more or less persistent bathing in toxic lymph. If the infection be active or the resistance low, or both, the pathogenic organisms may be carried into the muscle, giving rise to suppurative processes, such as have been described by Rohrer in the diaphragm, and figured in one of the preceding cases as occurring in the intercostal muscles. If the bacteria be scanty or of indifferent activity or the patient's resistance high, they remain in the lung or pleura, and the muscles escaping direct infection suffer from the toxic action only.

Where the irritation extends over a considerable length of time and granulation tissue with its protective influence against infection clothes the costal pleura, or where newly formed collagenous tissue is intercalated between the muscle and the altered serosa, then products reaching the muscle would probably be less active or materially modified toxins without evident bacteria. Here, then, results the chronic sclerosing change comparable to that seen in the muscles adjacent to tuberculous areas elsewhere in the body, as, for example, around tuberculosis of the hip, vertebræ, etc. In the more acute stages of the process the degenerative and necrotic change seen in the muscles may be attributed to the action of the toxins, passing through the lymphatics of the muscles or diffusing into the muscle tissue. In the later acute cases bacteria themselves enter. In the cases of longer duration there might occur a chronic suppurative interstitial and parenchymatous myositis, but probably the patient would not survive an infection of this type, except purely as a local manifestation. The chronic alteration of importance is the sclerosing process by which the muscle is in part or almost wholly replaced by newly formed fibrous tissue in which fatty infiltration or lipomatous substitution almost constantly occurs.

The influence of the changes already described on the thoracic wall so fully suggest themselves that a detailed consideration need hardly be given. The clinician will at once think of the modifications in physical signs—muffling and alteration in auscultatory sounds depending upon increased density of the thoracic wall—brought about by any of the changes described, including serous infiltration, cellular accumulation, as well as fibrous and lipomatous change in the intercostal muscles; the influence of the change upon the function of these muscles will also be apparent. Even slight myositis is associated with rigidity, a more or less successful attempt at fixation, and this fully accords with the recognized clinical data.

A large amount of space might profitably be devoted to consideration of the influence of the change upon respiration, but as this is evident, I need but touch upon this point. Hamberger's observations on the functions of the intercostal muscles in respiration has received general acceptance, and has been corroborated by the studies of Newell Martin and Hartwell, Masoin, and R. du Bois-Reymond.[1] The fact that the internal muscles are actively operative in respiration only when the function is labored renders more important the alterations now under consideration, because with alterations in the diaphragm, the principal muscle of respiration, and with the influence of intoxication upon the respiratory centres, and satisfactory evidence of narrowing of the intercostal spaces, as suggested by Przewalski, it becomes at once clear that structural alterations

[1] The details of muscular action in respiration are fully considered by Starling in Schäfer's Text-book of Physiology, vol. ii. pp. 274–280; he also cites the authorities to whom I refer.

in these muscles must materially influence the alterations in chest volume upon which air intake so largely depends. The fact that the external intercostal muscles are but slightly involved and often escape does not modify this observation, because physiologists are fully familiar with the fact that opposing muscles are reciprocally influenced. Mention should be made of the influence of sclerosing myositis in the production of costal fixation in the chronic cases; whatever views may be entertained with regard to the inexpansibility of lungs long atelectatic, the condition of the ribs as regards motility cannot be ignored. The fixation of the affected side in acute cases may be, as is usually held, reflex, but it may also depend upon the spastic fixation of muscles (intercostal and diaphragmatic), the seat of pronounced architectural change.

Structural alterations in the intercostal muscles possibly clear up to some extent the observations that intercostal rheumatism, intercostal neuralgia, etc., are complicating or associated phenomena of pneumonia and pleurisy. In this connection there are several factors in this field that the writer appreciates are not worked out. Probably the most conspicuous is alteration of the nerves. Some of the sections show nerves that appear œdematous. In none of them has any cellular infiltration been observed. The tissues have not been prepared suitably for the demonstration of myelin degeneration, and this question must be taken up with some detail later. I might at this point, however, say that sections show, what histologists so far as I know do not mention, namely, that nerve filaments or even relatively large trunks can be seen coursing between the internal intercostal muscles and the adjacent pleura. They are so situated as to expose them to all the toxic substances permeating the adjacent muscle. In one block of tissue from an acute case two relatively large nerve bundles can be seen immediately below the serosa imbedded in a small cushion of fat; the epineurium touches the serosa, and a vessel lying in immediate proximity contains, on transverse section, seventeen erythrocytes, two polymorphonuclear leukocytes, and one hyaline cell—presumably a local leukocytosis. The nerve bundle is retracted from its sheath, on the inner aspect of which can be recognized transverse sections of two capillaries containing red cells, but no leukocytes; there is no leukocytic infiltration of the sheath or nerve. Another specimen contains a longitudial section of a nerve that at one point shows a suggestion of cellular infiltration and contains a widely dilated capillary. Such axis-cylinder stains as have been applicable to Zenker material demonstrate no noteworthy change in the myelin sheaths and axis-cylinders of the nerves, but, as usual in such material, myelin stains have proved unsatisfactory.

The foregoing offers no sufficient anatomical basis for the conclusion that the nerves suffer; nevertheless, I am satisfied that in such instances as the one narrated they cannot long escape. Their

perilous situation exposes them to the noxious influences of infection, toxic bodies, and other coincidents of inflammation, to the action of which nerve elements are conspicuously susceptible. It would be interesting to know if the clinicians have observed any paralytic phenomena that indicate a toxic degeneration or neuritis involving the phrenic nerve or motor branches to the intercostal muscles. Alteration in the sensory fibres is strongly indicated by certain of the clinical factors; will the clinicians kindly advise us what, if any, symptoms or physical signs point to motor involvement? I feel reasonably certain that there is no sufficient reason why the motor nerves should escape.

An extremely important point to be determined is whether there are any lymphatic ways corresponding to intercostal spaces in which this change is most marked. While I have no information that would justify a positive conclusion upon this point, the fact that well-marked changes may be seen in one area of an intercostal muscle, and the block of tissue from an adjacent neighborhood fails to show the alteration, leads to the belief that the lymphatic course or tract should merit special consideration, and it appears that in a very general way only have the anatomists and histologists solved this problem. Possibly we have, in what might be called pathological injection of the lymphatic spaces and vessels, an important adjuvant in the study of the lymph courses. I have had no opportunity to study the changes in the lymph trunks draining the costal pleura; such a study, based upon experimentally produced inflammations of the lung and pleura, is needed.

An important question suggested by Dr. Riesman is what would the intercostal muscles of the sound side show? In one of the cases of pneumococcal pleurisy the muscles of the other side escaped, or at least showed no structural change. I am not inclined to believe that the opposite side is involved, unless thrombosis of the costal lymphatics of one side might lead to an anastomotic current passing to the other; such spanning of the mediastinum would seem improbable.

Another point upon which these studies are inadequate is the frequency with which the intercostal involvement occurs. Five of the seven cases studied are Philadelphia Hospital patients, and those familiar with the Blockley morgue know that we may draw incorrect conclusions as to the frequency of concurrent conditions, because we are dealing with a class in whom coincidence of pathological processes is a conspicuous feature.

Kuettner[1] has made an exhaustive study of the perforating lymphatics of the diaphragm. He shows that the drainage territories of the diaphragm are such that abundant opportunity is

[1] Thirty-third Congress of the German Surgical Society, June, 1903; Centralbl. f. Chir., 1903, No. 36; Beiträge z. klin. Chir., Tübingen, vol. xl., No. 1.

afforded for transdiaphragmatic infection, and has so worked out the lymph paths as to show that while each half of the organ possesses its own lymphatic field communicating with other parts by way of lymph nodes only, all parts of the diaphragm possess anastomotic communication with the pleura and peritoneum. The anterior and posterior lymph vessels communicate and drain in common into certain glands; some of these vessels vertically transverse the diaphragm twice in coursing over it. Taken with the studies of Rohrer and my own observations, it seems that Kuettner's work forms the necessary link in completing our already fairly full comprehension of the possibilities of transdiaphragmatic infections. That a juxtaposed abdominal viscus may infect the pleura or pericardium (*e. g.*, hepatic, splenic, and perirenal abscesses and gastric ulcer) has long been common property, but that lesions of a finer texture may be recognized, and that the four great serous cavities are really intercommunicating lymph spaces, is within recent times leading to deductions some of which may be important. Is it possible that the pneumococcal inflammations of the peritoneum (even when primary) may be transdiaphragmatic infections, the lung and pleura escaping in some cases? The frequency with which the ribs suffer typhoidal osteomyelitis is suggestive, and if, as Fraenkel holds, the typhoidal spondylitis is really a bacillary infection of the cancellous tissues of the bodies of the vertebræ, the demonstration of abdominal and thoracic lymph systems as so closely allied threatens, as the result of a minor disclosure, to lead one into a labyrinth of unjustified speculation.

It is not the purpose of this paper to consider transdiaphragmatic infections, the passage of fat-necrosing substances through the diaphragm, and cancerous extension from peritoneum to pleura, or the reverse; these subjects have recently been studied by von Brunn[1] and Jensen,[2] in pneumococcal peritonitis; by Henle,[3] in an article on "Pneumonia and Laparotomy;" by Truhart,[4] in considering intrathoracic fat-necrosis in disease of the pancreas, and by Tilger,[5] in pleurisy and peritonitis; Kuettner[6] discusses and gives most of the references. The demonstration of lesions in the tendon of the diaphragm is only a minor extension of Rohrer's observation.

In conclusion, I wish to express my appreciation of the kindness of Professor Keen, and Drs. Rosenberger, Ellis, and Funke, for helpful aid in the preparation of material upon which this paper is based.

[1] Beiträge z. klin. Chir., Bd. xxxix., Heft 1, p. 94.
[2] Langenbeck's Archiv, Bd. lxx., Heft 1, p. 95.
[3] Ibid., Bd. lxiv., Heft 2.
[4] Pankreas Pathologie, 1902.
[5] Virchow's Arch., Bd. cxxxviii. p. 499.
[6] Loc. cit.

A CLINICAL REPORT OF THREE CASES OF INJURY TO THE LOWER SPINAL CORD AND CAUDA EQUINA:

WITH REMARKS UPON PERONEAL PALSY DUE TO A LESION IN THE EPICONUS, UPON INCREASE OF THE PATELLAR TENDON REFLEXES FROM A LESION BELOW THE LUMBAR SEGMENT, AND UPON A RARE FORM OF BROWN-SÉQUARD PARALYSIS RESULTING FROM A LESION OF THE LOWER END OF THE SPINAL CORD.[1]

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(From the service of Dr. Wm. G. Spiller, Philadelphia and Polyclinic Hospitals.)

The following three cases are reported because of their unusual symptoms. The first case presents bilateral peroneal palsy with typical steppage gait due to a lesion in the epiconus—*i. e.*, that portion of the spinal cord between and including the fifth lumbar and first and second sacral segments. Peroneal palsy is almost always due to a peripheral lesion. The second case is one with increased patellar reflexes with a lesion in the cauda equina, below the reflex arc for the knee-jerk. This condition has not been heretofore dwelt upon. The third case is interesting because of a form of Brown-Séquard paralysis peculiar to cases of unilateral lesions in the lower end of the cord. In this type motion and sensation are affected in the same lower limb, while sensation in the external genitalia and perineum of the opposite side is also disturbed.

Case I.—J. K., aged thirty-five years, laborer, while walking on a railroad track was struck by an engine going at a moderate rate of speed. He was struck in the middle of the back and was thrown about thirty-five feet. He was picked up in an unconscious condition, and when admitted to the University Hospital two hours afterward consciousness had returned. He had always been healthy up to this time (January 5, 1901). His family history and past history are negative. Examination on admission showed numerous lacerations of the head, ears, a broken nose, and subconjunctival ecchymosis. The back in the mid-dorsal and lumbosacral region was contused, but no fracture or dislocation of the vertebræ could be made out. The man complained of intense pain in the back and of a burning sensation in his feet, which was aggravated by pressure. There was complete motor paralysis of his lower extremities. Vesical control was lost. No rectal disturbances were present. Examination

[1] Read before the Philadelphia Neurological Society, October 27, 1903.

three days after the injury by Dr. Potts gave the following results: The patient can voluntarily contract the quadriceps and adductor muscles of either thigh. He is able to raise the thigh slightly from the bed. No atrophy is noticeable in the lower extremities. All muscles respond to the faradic current. All the reflexes in both lower extremities—*i. e.*, the patellar jerk, Achilles jerk, and ankle clonus—are absent. Plantar irritation produces no movement of the toes. He cannot pass his urine voluntarily, but knows when his bladder is full. To-day he defecated voluntarily. Sensation for touch, pain, and temperature is lost over the dorsum of both feet, and on the outer side of both legs to the knees. He complains of an intense burning and numb feeling in both feet, especially marked when pressure is applied. He does not know when his toes are moved. A beginning bed-sore is found over the sacrum.

A note made twenty-five days after the injury states that vesical control was normal. Examination by Dr. Potts a month after injury gave the following results: the patellar jerks are still absent. The Achilles jerk is present on each side and is marked more on the right. Plantar irritation produces a doubtful extension of toes on both sides. The muscles are flabby and somewhat atrophied. No change in electrical reactions is found. Sensation is about the same as at the previous examination. From this time on his condition gradually improved, the patellar jerk on the left side returned two months later. Six months after the injury he was able to be out of bed and could walk with the aid of crutches, at which time it was noticed that he had a typical "steppage" gait. He left the University Hospital (April 30, 1902) and could then walk without the aid of a cane, and was admitted later to the nervous wards of the Philadelphia Hospital, service of Dr. William G. Spiller.

Examination on September 30, 1903, by me showed a wasting of the buttocks and of both lower extremities, more marked on the right side, there being a difference of one inch above and one-half inch below the knees. He lies with both extremities strongly abducted. Motor power is diminished on the right side more than on the left. The flexors of the right thigh are weak, while power of adduction of both thighs is greatly diminished, and more so on the right side. He can flex and extend the toes slightly, but no movements are possible at the ankle-joints, and he has bilateral foot-drop. The patient walks with a swinging step, lifting his foot high from the ground, and has a distinct steppage gait.

The cremasteric reflex is prompt on either side. The left patellar tendon reflex is much exaggerated; on the right side, however, there is no movement of the leg on the thigh from tapping the patellar tendon, but a strong contraction of the quadriceps muscle can be easily felt. Ankle clonus is prompt and persistent on both sides. Babinski's sign is present on either side. There is a hypæsthesia for all forms of sensation over the dorsum of both feet, extending on the

outer side of both legs to the knees. Bladder and bowel control are normal. All the muscles of the lower limbs respond to the faradic current.

The lesion in this case was most probably a hemorrhage into the spinal cord or a traumatic myelitis between the fourth lumbar and third sacral segments of the spinal cord. The absence of bladder, rectal, and sexual disturbances shows that the conus medullaris, arbitrarily put by Raymond between the beginning of the filum terminale and the third sacral segment, and including that segment, and that the fibres in the lateral columns controlling these reflexes are intact. The paralysis involves principally the peroneal group of muscles on either side, while the adductors and flexors of the thighs, especially on the right side, are paretic; in addition, there is a weakness of the glutei. The cells in the anterior horns of the spinal cord controlling these muscles have been placed by various authors between the fourth lumbar and third sacral segments, some writers placing the centres for the adductors and flexors as high as the third lumbar segment. The upper limit of the lesion is shown by the presence, in fact, the exaggeration of the patellar tendon reflexes and the preservation of the cremasteric reflex, these reflexes showing the integrity of the fourth lumbar segment and the lumbar segments above.

The case affords evidence that the cremaster reflex arc must have its spinal portion above the fourth lumbar segment, and that it is not in the sacral cord, as some writers have taught, and that the reflex arc for ankle clonus must be below the second sacral segment. The preservation of the bladder, rectal, and genital reflexes seems to indicate that the white matter of the lateral columns is not seriously affected, even in the lower lumbar and upper sacral cord, and that the lesion must be almost confined to the gray matter.

Minor,[1] of Moscow, pointed out in 1901 that just such a symptom-complex always occurs in lesions involving the gray matter of this area—*i. e.*, the fifth lumbar and first and second sacral segments. In such cases the paralysis always involves the distribution of the sacral plexus, and the peroneal group of muscles is most affected and the paralysis of these muscles lasts the longest. In some of his cases there was paresis of the flexors and adductors of the thigh. The negative symptoms were preservation of the patellar reflexes and absence of bladder and rectal disturbances. He called this region of the spinal cord the epiconus. Similar observations have been recorded by others, Remak,[2] Wagner and Stolper, Kötter, Barth and Hartmann, and Erb, but none by English and American writers, so far as I know. The important feature of these cases is

[1] Deutsche Zeitschr. f. Nervenheilkunde, 1901, p. 334.
[2] Quoted by Daus., S. Monatsschrift f. Psych. u. Neurol., B. xiii., H. 5, S. 394, 1903.

the involvement of the gray matter of the fifth lumbar, and first and second sacral segments with integrity of the white matter.

CASE II.—J. C., aged thirty-one years, white, laborer, was admitted to the Philadelphia Hospital July 13, 1903. He was shot June 8, 1903, in the left buttock with a thirty-eight calibre Colt revolver about ten feet away, the ball entering and perforating the left fifth lumbar vertebra, as was shown afterward by the *x*-rays. The course of the bullet was downward and to the right; the ball, however, has not as yet been located. The patient could not walk during the first two weeks and had no control of the bladder or rectum. Examination by Dr. Spiller, July 18, 1903, one month after injury, showed that voluntary power in the lower limbs was nearly normal, except in the flexors of the right foot. Both patellar jerks were a little prompter than normal. The Achilles jerk was absent on either side, and Babinski's sign was absent, there being no movement of the toes in either direction. There was an area of greatly diminished sensation for touch and pain over the right buttock, extending about three or four inches from the median line, and in a narrow zone back of the right thigh and back of the right leg, and on the outer side and sole of the right foot, corresponding, according to Kocher's diagram, with the distribution of the second, third, and fourth sacral segments. The sensation in the left lower limb was normal. He had incontinence of the bladder and bowel.

Examination by me October 11, 1903, three months after the injury, showed the patient's condition to be much improved. The flexors of his right foot were still weak and he could not rotate outward his right thigh as well as he should. The right buttock was flat, there being atrophy of the glutei. Sensation was about the same as at the previous examination, with the addition of a hypæsthesia of the right side of the scrotum and penis.

Both cremasteric reflexes were present, and both patellar tendon reflexes were distinctly increased. No Achilles jerk nor Babinski's sign was obtained on either side. He could hold his urine, but the power of the bladder was still diminished. He was constipated, and after a purgative could not control the rectum. All the muscles responded to the faradic current, except the right glutei, there being also no response in these muscles to the galvanic current.

The lesion in this case must have implicated the cauda equina, as the bullet entered at the fifth lumbar vertebra, and its course was downward. The interesting point of this case, and the one I wish to call special attention to, is the increase of the patellar tendon reflexes when the lesion was below the reflex arc. I have been unable to find any reference to this condition in the literature at my command, except in Thorburn's[1] contribution to the *Surgery of the Spinal Cord*. This author mentions the following cases with increase

[1] Philadelphia, Blakiston & Son, 1889.

of the patellar reflexes, but pays no special attention to this subject. One case I have found also reported by Franz Volhard.[1]

First case, cited by Thorburn from Kirchoff: backward crushing of the first lumbar vertebra causing a degeneration of the fourth and fifth sacral segments, the only symptoms being paralysis of the bladder and rectum and increased patellar reflexes. Sexual and sensory changes are not mentioned.

Second case: a partial compression of the cauda equina about the level of the last lumbar vertebra, causing severe neuralgic pains in the sciatic and pudic distributions, a weakness of some of the muscles of the lower limbs, but no complete paralysis and no anæsthesia of the limbs. The bladder and rectal functions were paralyzed. The patellar reflexes were slightly exaggerated, but there was no ankle clonus.

The third case is cited by Thorburn from Oppenheim, and was one of fracture of the first lumbar vertebra, causing a myelitis of the conus medullaris. There was a slight weakness of the calf muscles, otherwise no loss of power or atrophy. Anæsthesia was limited to the peroneal region and buttocks. There was paralysis of bladder and rectum. Here also the knee-jerks were exaggerated, but there was no ankle clonus.

The fourth case, by Volhard, of a tumor of the cauda equina, as proved by necropsy, with motor and sensory symptoms, absent Achilles jerks, and weakness of the plantar reflexes, but both the patellar reflexes and the cremasteric reflexes were exaggerated.

In all four of these cases, therefore, the exaggeration of the patellar reflexes was probably caused by lesions *below* the reflex arc.

It is difficult to find a satisfactory explanation for such a phenomenon as this, but evidently the patellar reflex arc is in some way thrown into a state of excitation in these cases. No writer has made this a subject of careful study, and it seems therefore important to emphasize the fact that a reflex may be increased by a lesion in the spinal cord below the portion in which the reflex arc is represented. Considerable evidence is offered that in the nervous system there are both depressomotor and excitomotor fibres for the different reflexes, these having their origin in the brain; and it may be that other excitomotor fibres exert their influence on segments above those in which these fibres arise. We know that spinal roots on entering the cord give off descending branches that pass downward in the posterior columns; the function of these fibres is entirely unknown, but we must assume that in some way they affect the function of the lower segments. It is probable that in a similar manner the lower spinal segments exert some influence over higher spinal segments, and there is no doubt whatever that in the anterolateral columns degeneration of short fibres occurs upward. It is

[1] Deutsche med. Wochen., 1902, No. 33.

presumable that these fibres exert some control over higher segments than those in which they arise, and in this way possibly cause an exaggeration of tendon reflexes.

CASE III.—S. W. was admitted to the Polyclinic Hospital July 15, 1903. He fell down an elevator-shaft from the eighth floor, a distance of about 120 feet. He was not unconscious, but sustained a fracture and displacement of the second lumbar and twelfth thoracic vertebræ, as determined by the *x*-rays several days afterward.

Examination by Dr. Spiller on the following day gave the following results: The right lower limb was completely paralyzed. Voluntary power in the left lower limb was almost normal; some weakness, however, was present in the flexors of the left thigh. The patellar jerks, Achilles jerks, Babinski's reflex, and ankle clonus were not obtained on either side. The cremasteric reflex was lost on the right side, but prompt on the left side. The bladder and bowel control was lost. The whole right leg felt numb. Sensation did not appear to be lost entirely in any part, but touch and pain sensations seemed impaired in the right thigh, both front and back, over the right buttock and the right side of the scrotum. The sensation of the left lower limb was normal.

Examination by me August 10, 1903, one month afterward, showed no appreciable change, except that by reinforcement a slight movement of the leg on the thigh was obtained on tapping the left patellar tendon. The whole right leg seemed wasted. He could flex the toes slightly, and bladder and rectal control was better. From this time on the patient improved steadily, and was discharged from the hospital September 1, 1903, about two months after admission.

Examination at present, three months after injury, gives the following results: The patient is able to walk without the aid of crutches, although still weak. The left lower limb seems normal. The right lower limb is generally wasted as compared with the left lower limb. All movements of the toes, ankle, knee, and hip on the right side are possible, although not quite normal. The patellar tendon reflexes, Achilles jerk, and ankle clonus are absent on either side.

Plantar irritation produces no movement of the toes. The cremasteric reflex is absent on the right and prompt on the left side. There is no absolute loss of sensation in the right lower limb, but he does not feel touch and pain as well as he should, and he complains of numbness in the anterior part of the thigh and foot. The bladder, bowel, and sexual functions are still impaired. Sensation is normal over the left lower limb, but touch and pain sensations are diminished over the left half of the penis and scrotum.

The interesting feature of this case is the Brown-Séquard symptom-complex, as shown by the weakness of the right lower limb and the

hypæsthesia for touch and pain in the same lower limb, while on the other side there is hypæsthesia for the same forms of sensation over the left side of the penis and scrotum. The lesion must have been a traumatic myelitis of the right side of the spinal cord or an intramedullary hemorrhage, sufficiently high to involve some of the motor and sensory fibres of the same side supplying the right lower limb, but not high enough to involve the sensory fibres supplying the left lower limb after their decussation to the opposite side. It has been shown that the sensory fibres of the pudendal plexus decussate lower in the spinal cord than do the sensory fibres supplying the lower extremities. This case seems to prove this view to be correct,

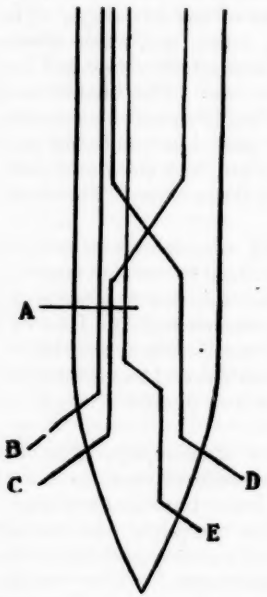

Diagram showing the motor and sensory fibres implicated within the spinal cord in Case III. A. Unilateral lesion implicating the lumbar and sacral regions below the line represented by A. B. The motor fibres of one side of the cord for the innervation of the lower limb. C The sensory fibres from the same lower limb, decussating above the lesion. E. The sensory fibres from the perineum and external genitalia of the opposite side, decussating below the lesion. D. The sensory fibres from the opposite lower limb, decussating above the lesion.

because there was hypæsthesia for touch and pain over the penis and scrotum and possibly over the perineum on the left side, opposite the side to that in which was the lesion, while in the left lower limb sensation was normal.

We may expect therefore in a case of unilateral lesion in the sacral and possibly the lower lumbar region of the spinal cord, disturbance of motion and sensation in the lower limb and in the external genitalia and perineum on the same side as the lesion, and disturbance of sensation in the external genitalia and perineum of the opposite side. This explanation for this symptom-complex is made more comprehensible by the accompanying figure. This is

a form of Brown-Séquard paralysis, but very different from that occurring when the lesion is higher in the cord.

This interesting symptom-complex was first described by Wernicke[1] in 1891. Later, Mann[2] described more fully the same case, and added a similar one of his own. So far as I know these two are the only previous cases on record. A short abstract of these cases is given below:

CASE I.—Patient, aged thirty-two years, had not had syphilis, and previously had been healthy. One evening he complained of intense pain in the back and a weakness in the left lower limb. This increased so that he could not use his leg at all. Pain disappeared shortly and paresis improved. Six months after this he presented a flaccid paralysis of the left lower limb; the only muscle acting was the iliopsoas. All the reflexes were lost. He never had bladder, rectal, or sexual disturbances and no pain in his left leg. Sensation for pain and temperature was diminished in the left lower extremity as compared with the right lower extremity. On the right side sensation for pain and temperature was diminished over the scrotum, penis, and perineum. No motor weakness was found in the right leg.

CASE II.—Patient fell three metres, landing on his buttocks. This resulted in a paralysis of the left lower limb, loss of sexual, bladder, and rectal control. One year after the injury the gait was spastic and paretic, the left leg being dragged on the floor. There was weakness of both lower limbs, much more marked on the left side; the patellar reflexes and Achilles jerks were much increased, but more on the left side. Ankle clonus was not obtained. Both lower limbs were flaccid on passive movement. On the left side there was hypæsthesia for pain and temperature up to the inguinal region anteriorly and iliac crest posteriorly. Touch sensation was normal. The right half of the penis, rectum, and perineum were hypæsthetic to pain- and temperature-sense.

Another interesting feature of my third case is the almost complete restoration of motion in the right lower limb, following probably a traumatic myelitis. In another case which I had the opportunity of seeing through the kindness of Dr. Spiller, paralysis in all four extremities following a jump out of a third-story window existed. Thirteen months after the injury examination showed hardly a trace of paralysis. Such cases as these show the wonderful recuperative powers of the spinal cord when destruction is not complete at any one level.

[1] Sitzungsberichte der schlesischen Gesellschaft f. vaterländische Cultur. Sitzung vom 6 Februar, 1891, ferner Gesammelte Aufsätze, p. 300.

[2] Deutsche Zeitsch. f. Nervenheilkunde, vol. x.

THE RELATION OF TYPHOID FEVER TO TUBERCULOSIS.

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It is well known that typhoid fever and acute tuberculosis may be rarely associated, and form, so to speak, a composite clinical picture. More commonly, typhoid fever develops in the course of chronic tuberculosis. When acute miliary tuberculosis and typhoid are concurrent, the former disease is, as a rule, secondary to the latter, although it must be recollected that an old tuberculous focus usually co-exists.

In other words, these are cases in which persons with either an active chronic tuberculosis or a latent encapsulated focus contract typhoid fever. It may be assumed that the reaction of the tissues is incomplete; that the resisting powers are defeated and the bacilli liberated under the influence of the typhoid infection. It is also clear that forms of acute tuberculosis are not likely to supervene when there is present a thick, dense limiting wall as in old cases that are practically cured.

This paper deals principally with typhoid fever complicated with acute miliary tuberculosis and acute pneumonic phthisis. It is important to bear in mind that the typhoid process is responsible, in the manner explained above, for the rapid dissemination of the tubercle bacilli or the conversion of chronic into acute tuberculosis.

It must be admitted that rapid infection of the lungs with tubercle bacilli from without may also occur in the course of typhoid fever and acute pneumonic phthisis result as a complication, the primary infection serving as a predisposing condition. Indeed, in at least 4 of the six cases of combined typhoid and acute tuberculosis reported below, the latter affection assumed the pneumonic type, and some of these at all events may have been due to this mode of infection. Moreover, it must be recollected that when typhoid fever arises in subjects of arrested pulmonary tuberculosis and is complicated with bronchopneumonia (as was true of Case II. of my series) the inflammatory changes occasioned by this complication may break down the protecting wall and allow of the distribution of the tubercle bacilli throughout the lungs as well as to other and more remote regions by means of blood and lymphatic metastasis.

It does not appear that a chronic tuberculous process predisposes markedly to typhoid fever, judging from the comparative infrequency of enteric fever in the course of that common disease. Thus out of a totality of 249 autopsies in cases of typhoid fever, only 19 (7.6 per cent.) showed the presence of old tuberculous lesions. Per contra, the former widespread opinion that typhoid

fever predisposes to tuberculosis receives no support from my observations, as will be shown hereafter.

Eshner[1] has reported a case of triple infection—pulmonary tuberculosis with intercurrent typhoid fever complicated by pneumonia—and, bearing upon the subject of the occurrence of typhoid fever in the course of tuberculosis, he makes the following statistical quotations: "Among 2000 fatal cases of typhoid fever examined after death at Münich, Hölscher noted 108 (5.4 per cent.) of tuberculosis in various situations, and he quotes Gruber as having noted, among 710 fatal cases of typhoid fever, 22 (3.3 per cent.) complicated by old tuberculosis of the lungs. Bettke, among 1420 cases of typhoid fever at Basle, noted 23 (1.6 per cent.) in tuberculous subjects; while Dopfer noted tuberculosis in 46 (5 per cent.) among 927 cases of typhoid fever."

No allusion is made to the association of acute forms of tuberculosis with typhoid fever in these statistical representations. M. Forget[2] affirms that persons suffering from pulmonary tuberculosis are rarely attacked by typhoid fever, and regards the former as preservative against the latter.

The question of the diagnosis of these combined affections is of the utmost importance from the standpoint of prognosis, the outlook in pure typhoid being generally hopeful. I have also endeavored to determine the incidence of the hybrid affection—typhoid fever and acute tuberculosis—which, as will be shown hereafter, is fortunately extremely rare. The writer has recently met 2 cases in his hospital practice in which these two leading affections appeared to be concurrent. The post-mortem records of the Philadelphia and Episcopal Hospitals for the last ten years have been carefully examined with reference to the question of the relation of typhoid fever to tuberculosis, and the results have been tabulated as follows:[3]

	Total number of cases showing typhoid lesions.	Number of cases showing both typhoid and tuberculous lesions.	Number showing		Variety of acute tuberculosis.
			typhoid and chronic tuberculosis.	typhoid and acute tuberculosis.	
Philadelphia Hospital.	90	11	10	1	Acute miliary tuberculosis.
Johns Hopkins Hospital.	80	4	3	1	Acute pneumonic phthisis.
Episcopal Hospital.	79	8	6	2	Acute pneumonic phthisis and miliary of lungs and pleuræ.
Summary	249	23	19	4	

[1] Philadelphia Medical Journal, March 25, 1899.

Quoted by Murchison, The Continued Fevers of Great Britain, third edition, London, 1884.

[3] The writer desires to make grateful acknowledgment to Dr. Wm. Egbert Robertson and Dr. Ralph H. Spangler for kind aid in collecting statistical data.

Cases illustrative of combined typhoid and acute pneumonic phthisis and acute miliary tuberculosis.

CASE I.—L. B., aged twenty-five years, colored, unmarried, and by occupation a domestic; no history of the use of alcohol, but has had syphilis and one miscarriage; menstruation was regular as a rule.

Family History. Father deceased of unknown cause; mother of pneumonia; patient statedth at she was sick all of last winter; she died in spring; patient had never had any brothers or sisters.

Personal History. Whooping-cough, measles, and mumps as a child; at eighteen years had an attack of rheumatism lasting two weeks and making good recovery. Colds and "coughs" have been common during second decade of life; also sore throat, and much headache.

Present Illness. August 23d went to Cape May and contracted a "cold," which became persistently worse, and she was obliged to betake herself to bed. On September 8th patient was admitted to the female wards of the Medico-Chirurgical Hospital with a cough, pain in her left axillary region, fever, etc.

Physical Examination. Young colored woman, medium size, with poor development and slightly emaciated. There are visible a considerable number of punched scars on the anterior surface of leg. Knee-jerks normal; sensation normal; eyes, liver, and heart also normal. Spleen somewhat enlarged; consolidation of lower lobe of left lung, with a small cavity in left upper lobe.

September 18, 1903, 5 P.M. On account of the splenic enlargement the blood was tested for the Widal reaction, and it responded positively. A sero reaction was also obtained on September 20th and again on September 30th; the diazo reaction was present; considerable enlargement of spleen. Cardiac impulse weak and diffuse pulsation felt over region of left auricle. Slight increase of dulness over same region, but no murmur detectable. Patient much distressed; feels certain that death is at hand. Has at no time been delirious, but symptoms of motor irritation were noted as tremor of upper lips and hands.

Blood Examination. Hæmoglobin, 75 per cent.; reds, 4,680,000; whites, 9400.

Urine Examination. Granular casts; albumin, a trace; specific gravity, 1012.

21*st*. *Sputum Examination.* Tubercle bacilli present; also elastic tissue.

There would appear at first sight to be no doubt as to the coexistence of typhoid fever and acute pneumonic phthisis in this case. The earlier examinations of the patient after admission into the hospital all seemed to indicate tuberculosis; the sole feature that directed attention to the typhoid infection was some considerable splenic enlargement—a more marked increase in size than I

had ever seen in pure acute pneumonic phthisis. This fact suggested the making of a blood examination for the Widal reaction and led to the discovery of the associated disease—typhoid fever. Other symptoms of enteric fever, however, developed subsequently.

CASE II.—J. S., aged twenty-eight years, a Polander, single, laborer, was admitted to the Medico-Chirurgical Hospital October 29, 1903. The family history proved negative, and the same is true of his previous personal history. Patient was well developed and well nourished on admission; he was rational, though considerably prostrated and temperature 102° F.; spleen enlarged and two rose-colored spots visible. In addition, there are noted bluish spots, the "taches bleuatres" of the French writers, ranging from one-third to one-half inch in diameter and scattered over the entire body; they do not disappear upon pressure. A noticeable enlargement of the postcervical or epitrochlear glands can be detected; the penis shows an old linear scar beneath the frenum. There is slight rigidity of neck, but no tenderness along spine, scalp or head; the conjunctivæ are injected, the pupils slightly dilated. The gums are inflamed at the teeth, and bleed upon the slightest touch, and the pharynx is the seat of a decided catarrhal irritation. Numerous moist rales are heard over both lungs, more especially at right base, where the breath sounds are also bronchovesicular, showing lobular infiltration. Heart normal, although pulmonic sound is slightly accentuated. The spleen is enlarged; the abdomen not tender, but somewhat tympanitic with gurgling to pressure in right iliac region.

November 4th. General symptoms increased in severity; eruption characteristic and abundant; had rigor previous night, and later slight intestinal hemorrhage. The physical signs indicate resolution in right lower lobe of the lung. A bandage applied to right elbow after taking a blood culture produced ecchymosis of right forearm. Has marked hiccough, and is delirious.

12th. The physical signs indicate an area of consolidation in left lung near the base, and also one on right side at angle of scapula (bronchopneumonia). The sputum is tenacious, and decidedly hemorrhagic, and has been so for twenty-four hours; it shows no tubercle bacilli but streptococci and staphylococci. The urine analysis revealed the findings of an acute hemorrhagic nephritis.

15th. Small mass is noted in lower right quadrant of abdomen, below (?) the seat of the appendix. It is soft and presents fluctuation, and is slightly painful to touch.

18th. Patient's general condition has improved, although a large hemorrhage occurred last evening, accompanied by the usual drop in temperature. The palpable mass in abdomen is still present without change; the surgeon refuses to operate on account of extensive bronchopneumonia. The sputum is viscid, and tinged with specks of red blood. Signs of resolution slowly progressing in right lung.

December 10th. Since former note, numerous examinations of the sputum were made, with the same result as noted above. The Widal reaction was noted a few days after admission, and on several occasions during the course of the illness; the diazo reaction was also present.

11th. The physical signs indicated the presence of a small cavity in the left interscapular space. It was thought that an abscess had developed, but the sputum examination on the following day showed the presence of numerous tubercle bacilli for the first time, but subsequently they were constantly present and the temperature became hectic in type. The conclusion was now inevitable that tuberculosis had probably been associated with typhoid fever, and only declared itself during early convalescence.

The next case herein reported occurred in the Philadelphia Hospital, and is taken from the post-mortem and clinical records of that institution; it is the only instance of combined diseases under consideration out of 90 autopsies on cases of typhoid fever and on all cases of acute tuberculosis covering a period of ten years.

CASE III.—G. K., aged twenty-one years, white, single, laborer, admitted April 18, 1899. The history sheet was lost, but a few ward notes were found; the temperature averaged from 102° to 103.2° F., pulse 72, later frequent; respirations about 26; the spleen was enlarged, the abdomen was tympanitic and diarrhœa was present; sero reaction present; tubercle bacilli absent at first, later found; no mention of rose spots. Condition grew progressively worse, and patient died May 21, 1899.

The autopsy showed intestinal perforation with adhesions to the omentum. Typhoid ulcers in large intestine cicatrizing; also ulcers about the valve with swollen solitary follicles. Peyer's patches in stage of infiltration and ulcers very numerous.

The left lung is almost entirely free from pigmentation; the anterior portion of lung normal, except a few tubercles scattered through the apex; posteriorly, there are patches of pneumonia, involving about one-half the depth of the entire posterior portion of lungs. Right lung: upper lobe, normal; middle lobe is tubercular throughout, being consolidated to a considerable extent with many tubercles; lower lobe shows hypostatic pneumonia almost throughout.

The post-mortem records of the Episcopal Hospital furnish two instances of combined typhoid fever and acute tuberculosis, as follows:[1]

CASE IV.—J. McI., aged eighteen years, single, was admitted to the medical wards of the Episcopal Hospital August 30, 1898, and died September 12, of the same year.

The clinical diagnosis was typhoid fever with perforation. The

[1] The writer regrets that no clinical notes of this case are available.

autopsy, however, showed acute miliary tuberculosis in addition to the typhoid lesions with perforation. Both lungs were studded throughout with miliary tubercles, but there was no consolidation. The spleen was enlarged, and the small intestines presented typhoid lesions in the usual seat associated with marked hyperæmia. Perforation had taken place in the ileum, around which there was an adhesive, localized peritonitis. Many of the lesions were about to show necrosis.

CASE V.—On admission, the diagnosis of typhoid fever accompanied the patient, but the clinical diagnosis during the stay in the hospital was pulmonary tuberculosis and tubercular bacilli were found in the sputum. The case proved fatal, and loculated, serofibrinous, and hemorrhagic pleurisy was noted at autopsy; also caseous deposits and miliary tubercles throughout lungs and pleura, while the intestines presented typical typhoid ulcers. In this instance of combined typhoid fever and acute tuberculosis both affections had been, although at different times, diagnosticated during life, but their association was not recognized.

CASE VI.—Osler has informed me that out of a total of 80 autopsies of cases of typhoid fever at the Johns Hopkins Hospital, one showed acute tuberculosis starting in as an acute pneumonic condition.

It is evident from the foregoing statistical facts including the reports of the 5 cases, that combined typhoid infection and acute tuberculosis, as stated above, is rare. Thus acute tuberculosis was associated in 1.6 per cent., and chronic tuberculosis in 7.6 per cent. of the cases of typhoid that came to autopsy. I have not included case histories (except Nos. 1 and 2), unsupported by post-mortem proof, for the reason that the chances of error in diagnosis are exceedingly great, as will appear hereafter.

It is said that when tuberculosis and typhoid fever are associated together in the same case, the former may dominate the scene and cause the Widal reaction either to disappear or to fail to appear. For this reason, certain cases of the combined disorders may be readily overlooked.

E. Kraus[1] found in 1 case that a complicating pneumonia caused the sero reaction to disappear just one day prior to the death of the patient. The post-mortem revealed the lesions of typhoid and lobar pneumonia in combination. It would appear from this fact that the serum of some other disease like pneumonia and acute tuberculosis may prevent the reaction of the typhoid bacilli. It is possible that the sero reaction of typhoid fever is sometimes also delayed on account of interfering complications, or again, it may be temporarily absent in the course of a given case for the same reason. A careful study of the cases reported in the literature will reveal

[1] Zeit. f. Heilk., Bd. xxi., H. 5,

much evidence to support this view. Thus cases complicated with appendicitis at times, as I know from personal observation, do not show the Widal reaction until the complication is removed by operation.

Conversely, F. Lobiesen[1] examined the blood of 151 patients who did not have typhoid fever, but were admitted into the hospital with that diagnosis or suspected enteric fever. Of these 4 gave a positive reaction at 1 to 25, and 3 died, showing respectively acute miliary tuberculosis, retroperitoneal abscess and calculous pyelitis with tuberculous meningitis. He, with Fiocca,[2] concludes that a positive diagnosis can be made when the reaction occurs with a dilution as great as 1:50. Now, in Case I. of my series the blood examinations were made by the Bacteriological Department of the Bureau of Health, where the higher dilutions (1:40 to 1:50) are employed. It was deeply regretted that no autopsy was allowed, and yet, as stated above, there can be little room for doubting the coincidence of typhoid fever and acute pneumonic phthisis in view of the three positive sero reactions at intervals of several days. There was absolutely no history of previous typhoid infection.

If the Widal reaction can be relied upon to differentiate typhoid fever from acute tuberculosis with absolute certainty, then these two diseases were associated in this instance. In 2 of the cases reported below, however, in which the sero reaction occurred, the necropsy failed to show any typhoid lesions.

A number of recent observers have found that icteric serum was possessed of a certain amount of agglutinizing power. The subject has just been carefully reviewed by E. Libman.[3] He quotes Koehler, who found in 8 cases of icteric diseases of the liver an agglutination reaction in 6. The highest dilution in which he obtained the reaction was 1:40; very rarely 1:50, and once it was only 1:10. Koehler experimented with the bile of rabbits which had slight agglutinizing power; also with that of dogs, and this manifested a decided agglutinizing potency (even up to 1:160).

Libman[4] made observations upon ten specimens of human bile, either normal or from cases of typhoid fever, chronic pancreatitis or cholelithiasis, and in no instance could he get a positive Widal reaction. Sailer[5] reports 3 cases of intense jaundice, all of which failed to give the sero reaction. The time has arrived when a *slight reaction* in a dilution of 1:50 is not to be regarded as a positive Widal reaction.

It is admittedly difficult to interpret the clinical phenomena of the combined diseases during life. All of the cases that came to autopsy showed that the clinical diagnosis was either incomplete

[1] Zeit. f. klin. Med., D. V. L. 111, Heft 1 und 11.
[2] Il Policlinico, November 1, 1900.
[3] Medical News, January 30, 1904.
[4] Loc. cit.
[5] Transactions of the Philadelphia Pathological Society, 1902, p. 253.

or erroneous. In Cases I. and II. (see *ante*) acute pneumonic phthisis was associated with typhoid fever, and in the former a lobar type of consolidation occurred, while in the latter it was a bronchopneumonic type.

The question of the effect of acute tuberculosis upon the course of typhoid fever is one of considerable interest. It was observed in Case I. that the typhoid fever was apparently uninfluenced by the tuberculous process. Indeed, it may be said that the symptoms of typhoid were distinctly in abeyance. In Case II. the clinical features of typhoid were intense and the course prolonged, and yet this disease was a thing of the past before the tuberculous process reached the stage of cavity formation, and tubercle bacilli found in the sputum.

The temperature-curve in the combined cases resembled closely that of typical typhoid—at all events until the typhoid process had spent its main force. On the other hand, the pulse partook during the fastigium more of the character of that seen in acute tuberculosis than of typhoid fever, being rapid and feeble.

The diagnosis of the combined affections may be assisted by remembering that the characteristic typhoid symptoms usually manifest themselves before the diagnostic evidences of acute tuberculosis. This is particularly true of the cases in which the pneumonic type of a tuberculous process is associated with typhoid. Here the diagnosis cannot be completed, as a rule, until tubercle bacilli are discovered in the sputum usually after the lapse of weeks. In my cases no tubercle bacilli were detected until the physical signs denoting apical cavity formation were noted. In this connection, attention should again be called to the fact that in the majority of the cases the associated tuberculosis assumes the form of acute pneumonic phthisis, according to the results of my collective investigations. Certain forms of acute tuberculosis were commonly mistaken for typhoid fever, such as acute miliary tuberculosis and the acute pulmonary varieties, as the reports of the following cases will illustrate:

In November, 1901, I had under my care a patient in the Medico-Chirurgical Hospital suffering from typhoid fever, and who gave a strong family history of pulmonary tuberculosis. The case began with pleuritis, accompanied with moderate effusion. The diagnosis of tuberculous pleurisy was provisionally made, but after the lapse of ten days true typhoid symptoms supervened, while the effusion was slowly and gradually absorbed. Recovery ensued.

An interesting and instructive case is recorded by Osler,[1] in which for nearly two weeks tuberculous pneumonia was suspected on account of apparently clear physical signs and the family history. Later, the true typhoid symptoms appeared and became well

[1] Studies in Typhoid Fever, series 3, p. 464.

marked, although the Widal reaction was not present until the end of the third week.

The following two case histories bearing on this point have been taken from the clinical and post-mortem records of the Philadelphia Hospital:

CASE I.—S. R., aged twenty-two years, Polander, occupation laborer, was admitted to the medical wards of the Philadelphia Hospital April 26, 1902; a chill one week before, followed by dyspnœa, cough, bloody expectoration, intestinal disturbance, and mental dulness. No family history obtainable. The physical examination showed coated tongue, dicrotic pulse, broncho-vesicular breathing, and impairment of resonance over lower lobes. The abdomen was distended and tympanitic; spleen enlarged; few suspicious rose spots observed; temperature ranging from 102° to 104° F.; pulse 66 to 100; no positive Widal reaction; diagnosis of pulmonary tuberculosis was made during life.

The autopsy revealed typical typhoid ulcers, acute splenic tumor, parenchymatous degeneration of the liver and kidneys, and congestion of the lungs. On section, the lung texture showed slight increase of consistency, but crepitation was everywhere present. Typhoid ulcers were found in the ileum, and several large ulcers in the cæcum.

CASE II.—C. S., aged thirty-six years, a patient in the medical wards of the Philadelphia Hospital, died February 6, 1902. The history of the case was as follows: Ill three weeks with chill, cough, slight expectoration, occasional vomiting, some abdominal pain, diarrhœa, with bloody stools twenty-four hours after admission; temperature 104° F. Patient passed into the typhoid state, but no rose spots and no splenic enlargement was detectable. On percussion the bases of the lungs showed dulness, and on auscultation crepitant rales were heard over both lungs. A trace of albumin was found in the urine; the sputum showed no tubercle bacilli; Widal reaction not mentioned. The diagnosis during life was acute tuberculosis.

The post-mortem revealed typhoid ulceration of the intestines, acute splenic tumor, hyperplasia of mesenteric and other lymph glands, œdema of lungs and apparent parenchymatous degeneration of the kidneys. The lungs, it may be mentioned, showed increased consistency, and on section a dark and blood-stained fluid exuded upon pressure; no evidence of consolidation, and bronchial lymph glands negative.

Typhoid fever may be mistaken for tuberculosis, as shown by the following illustrative cases:

CASE I.—J. P., aged twenty-five years, colored, laborer, admitted April 23, 1899; family history negative; had malaria one and pneumonia three years previously. Present illness began two weeks ago with typical prodromes of typhoid; a few days later was seized with

pain in left side, and cough with slight expectoration. The above symptoms lasted until admission, after which he had two or three stools daily; also high temperature of irregular type; pulse small, frequent, and little tension; slight albuminuria; a few dry rales at end of inspiration. The Widal reaction was present and a few tubercle bacilli were found in sputum. The clinical diagnosis had been typhoid fever and tuberculosis.

The patient died twenty-eight days after admission, and the necropsy showed only tuberculous lesions, the intestines being normal (not injected even); tuberculosis of the mesenteric, retroperitoneal and periaortic lymph glands, and a small nodule in the liver. Miliary tuberculosis in lungs and spleen. Pathological diagnosis was chronic followed by miliary tuberculosis.

It will be noted that the sero reaction was found in this case without the presence of any discoverable typhoid lesions. It must be recollected, however, that cases of typhoid septicæmia occur in which there may be an utter absence of characteristic intestinal ulcers. It is with considerable unreadiness that I place on record this case and the following, both of which tend to disprove a dictum which has been generally accepted, while searching for data to show the interrelation of these affections.

Case II.—H. M., aged twenty-four years, occupation brakeman, was admitted to the male medical wards of the Philadelphia Hospital August 2, 1903. Family history negative; the patient had always been healthy except that he contracted syphilis two years previously. He was a confirmed alcoholic and an excessive smoker. On admission, was thought to be intoxicated, and taken to the "drunk ward," but the symptoms and appearance did not portray drunkenness; he was semiconscious, although in muttering delirium. It was learned that he had been indisposed for two weeks with anorexia, headache, increasing prostration. The spleen was slightly enlarged; the diazo reaction negative, Widal positive, and a few suspicious spots were noted on the back; the physical signs seemed to indicate lobar consolidation, and the respirations were as high as 40 per minute. A clinical diagnosis of typhoid fever complicated with pneumonia was made.

The patient died August 12, 1903. An autopsy revealed encysted pleural effusion and miliary tuberculosis; the intestines showed no macroscopic changes.

Case III.—C. H., aged twenty-five years, admitted to the Philadelphia Hospital March 20, 1900. Nothing could be gleaned regarding either the family or personal history. Said to have been ill two weeks, beginning with headache, malaise, diarrhœa, and high fever, but no cough. Physical examination shows tenderness, and gurgling in right iliac fossa, splenic region tender, but spleen not palpable. On sixth day after admission he became delirious, spat up a couple mouthfuls of blood; next day passed a quantity of dark

blood with stool. The urine contained both albumin and tube casts; the temperature ranged from 101° to 102° F. for six days, then from 99° to 100° F. until death, which occurred March 28, 1900.

The clinical diagnosis was typhoid fever. Post-mortem examination revealed acute tuberculosis; left lung rather firm, but crepitant throughout; no tuberculous cavity or nodes. Right lung at apex showed marked tuberculous change; spleen normal in size; the intestines showed numerous tuberculous ulcers.

CASE IV.—C. L. G., female, aged thirty years, died April 9, 1899, at the Episcopal Hospital (no bedside notes obtainable). A clinical diagnosis of typhoid fever was made, but the pathological findings showed the following: Lungs riddled with miliary tubercles, although no source of infection was discoverable; neither caseation nor cavities were observed. Bronchial glands slightly enlarged, but not broken down; the spleen weighed 6½ ounces, was very soft and friable, with some miliary tubercles scattered through its surface. The intestines were perfectly normal; the peritoneal surface of the bladder and uterus was studded with a few tubercles.

CASE V.—Patient was admitted to the medical wards of the Episcopal Hospital believed to be suffering from typhoid fever. The disease ran an acute course and proved fatal. At autopsy, miliary tuberculosis following chronic pulmonary tuberculosis, with cavity formation in lungs and also intestinal tuberculosis, was found.

CASE VI.—On admission, this case was diagnosticated as typhoid fever, but had typhoid six years previously. The Widal reaction was present; leukocytes, 10,400. Blood cultures were made, but did not show typhoid bacilli, and lumbar puncture failed to elicit fluid. The necropsy showed acute meningitis, especially at the base, associated with pleural adhesions, cavities in both lungs, and tuberculous ulcers in the intestines.

The question here arises, Was the Widal reaction in this case due to the attack of typhoid fever which had occurred six years previously?

Osler[1] has reported 3 interesting cases of the sort in which at the outset typhoid fever was strongly suspected, although the positive signs of this disease were absent, and the certain features of pulmonary tuberculosis finally supervened. In 1 of the cases, as is usual, rapid progress was made during lactation and the fever was mistaken for typhoid.

While it is important to recognize these two leading affections when combined, remembering the extreme rarity of the association, it becomes a matter of greater clinical importance to distinguish between typhoid fever and the various forms of acute tuberculosis, since they are so commonly confused with one another. Acute miliary tuberculosis may simulate typhoid fever so closely as to

[1] Loc. cit.

offer the greatest clinical difficulty. The absence of the Widal reaction, of the characteristic eruption and of the comparatively slow pulse in miliary tuberculosis, are to be especially noted. On the other hand, in cases in which strong suspicions of the existence of acute miliary tuberculosis are entertained, a careful search for tubercles in the choroid, and tubercle bacilli in the blood and sputum (if there be any), is to be carried forward. C. Loeb[1] has recently emphasized the value of ophthalmic examinations in the differential diagnosis between typhoid fever and acute miliary tuberculosis. The personal history is often most helpful. In doubtful cases an attempt should be made to cultivate the typhoid bacilli from any suspicious eruption that may be present. There are not a few cases in which a positive diagnosis, however, must be withheld, for lack of discriminating features.

DISTRIBUTION OF THE ULCERS IN TYPHOID FEVER.

By Joseph Louis Baer, S.M.,
of Chicago.

(From the Pathological Laboratory of the University of Chicago and Rush Medical College.)

The occurrence of two cases of typhoid fever with an unusual distribution of the ulcers suggested the desirability of a general investigation of the distribution of ulcers in this disease. The two cases are presented in detail, and are followed by an analysis of a series of 89 cases, and by a review and discussion of the literature on the subject.

The first case showed ulcers in the œsophagus and colon, and in no other part of the alimentary tract:

Case I.—This series 33; Rush Medical series 945. A. B., male, aged twenty-four years; died January 31, 1901.

Clinical Diagnosis. Typhoid fever; tonsillitis; pharyngitis; laryngitis; pleuritis; probable pneumonia.

Anatomical Diagnosis (Dr. H. G. Wells). Typhoid fever (colotyphoid); ulcerative colitis; follicular enteritis; swelling of mesenteric lymph glands and spleen; follicular pharyngitis; œsophageal ulcers; acute serofibrinous pleuritis; bronchopneumonia; fibrous perisplenitis and perihepatitis; healed pulmonary tuberculosis.

Tongue. Lymphoid follicles prominent.

Pharynx and Epiglottis. Covered by mucopus.

Œsophagus. Covered by thin mucopus. There are prominent follicular swellings. At a point 1 cm. below the cricoid cartilage is

[1] Archives of Ophthalmology, New York, 1903, vol. xxxii. pp. 453–469.

a superficial ulcer 5 mm. in its long diameter, which is parallel to the axis of the œsophagus. Near this are three smaller ulcers; floor smooth, margins sharp, outline oval, long axis vertical.

Larynx and Trachea. Covered by thin mucopus. No ulcers.

Stomach. No ulcers.

Small Intestines. There is a slight hyperplasia of the solitary lymph follicles, especially in the lower part. Peyer's patches are normal. There is some hyperæmia. No ulcers.

Large Intestine. Beginning at a point 30 cm. below the ileocæcal valve and extending 70 cm. are twenty-five ulcers, 2 mm. to 6 mm. in diameter, with swollen, elevated edges. None have perforated. There is some hyperæmia and hyperplasia of the lymph follicles.

Bacteriology. The typhoid bacillus was isolated from the heart's blood and kidney.

In the second case the ulcers were limited strictly to the ascending and transverse colon, the sigmoid flexure, and rectum.

CASE II.—This series 45; St. Luke's Hospital 38. E. T., male, aged twenty years; died and examined February 24, 1903.

Clinical Diagnosis. Typhoid fever; hypostatic pulmonary congestion; pseudohypertrophic muscular atrophy.

Anatomical Diagnosis (Dr. H. G. Wells). Typhoid ulceration of the colon; hypertrophic pulmonary emphysema; purulent bronchitis; bronchopneumonia, and left hypostatic pneumonia; œdema of the right lower lobe; acute lymphadenitis, peribronchial and mesenteric; hypoplasia of the aorta; hypertrophy of the left ventricle; parenchymatous degeneration of the liver and kidneys; fibrous pericholecystitis; atrophy of vermiform appendix; hyperplasia of the spleen; calcification of the peripancreatic and mesenteric lymph nodes; chronic diffuse nephritis; decubitus; hypoplasia of the testicles; fibrous increase in the thyroid; atrophy of the muscles of the lower extremities, with replacement by fatty fibrous tissue; contractures of the feet.

Œsophagus. The lymphoid nodules are prominent, but none are ulcerated.

Stomach. The mucous membrane is contracted, but the folds can be pulled out. No ulceration.

Duodenum. Lymphoid structures are prominent.

Lower Small Intestine. The last Peyer's patches are slightly swollen. A few irregular pigmented spots are found above the swollen Peyer's patches.

Large Intestine. Immediately below the ileocæcal valve is an ulcer 1 cm. in diameter. In the upper 30 cm. of the large bowel are five ulcers, the largest 2 cm. in diameter. There are also a few pigmented spots. 50 cm. below the valve are two ulcers, 1.5 cm. in diameter; 20 cm. farther another ulcer is found, 1 cm. in diameter; 35 cm. above the anus is an ulcer, 5 mm. in diameter; 10 cm. above the

anus three ulcers are present, placed parallel, 3 cm., 2 cm., and 1 cm. in diameter, and transverse to the long axis of the bowel.

The series of 89 cases whose analysis is presented here was obtained from two sources, 44 cases from the Cook County Hospital, June, 1897, to June, 1903, and 45 cases from the Presbyterian Hospital, August, 1895, to July, 1902.

The distribution of the ulcers is as follows:

	Cases.	Percentage.
Mouth	0	0
Larynx	3	3.4
Trachea	1	1.1
Pharynx	0	0
Œsophagus	1	1.1
Stomach	2	2.2
Duodenum	0	0
Jejunum	1	1.1
Ileum	67	75.3
Ileum, lower half	32	35.9
Ileum alone	29	32.6
Meckel's diverticulum	1	1.1
Small intestine (not specific)	12	13.5
Total cases of involvement of small intestine	77	86.5
Ileocæcal valve	1	1.1
Vermiform appendix	1	1.1
Cæcum	15	16.9
Ascending colon	13	14.4
Transverse "	12	13.5
Descending "	5	5.6
Colon (not specific)	12	13.5
Sigmoid flexure	3	3.4
Rectum	3	3.4
Large intestine (not specific)	9	10.1
Large intestine alone	5	5.6
Cæcum alone	2	
Cæcum and ascending colon	1	
Cæcum and appendix	1	
Ascending colon, transverse colon, sigmoid flexure, and rectum	1	
Total cases of involvement of large intestine	45	50.6
No ulcers (with bacteriology)	2	2.2

Comparison of the percentages of distribution of the ulcers derived from this series with those derived from the general statistics in the literature, and which are presented later, reveals a close correspondence, except in two important items: In this series the percentage of involvement of the small intestine (in any part), 86.5 per cent., and of the ileum, 75.3 per cent., is markedly lower than the figures obtained from the older statistics, 99.4 per cent. and 89.9 per cent., respectively; while, on the other hand, the involvement of the large intestine in this series, 50.6 per cent., is more than double the percentage derived from other statistics—*i. e.*, 22.7 per cent.

This difference seems to me to indicate careful examination at the autopsies in this series, rather than variations that are the result of chance, and this explanation is further borne out by the fact that the same differences, though in less degree, exist between the earlier and the more recent statistics in the literature.

The bacteriology has been recorded in 37 of the 89 cases.[1] The typhoid bacillus, with or without other organisms, was found in 31 cases. Other organisms only were recovered in 6 cases.

Perforations were found in 14 cases (15.7 per cent.), distributed as follows: ileum, 9 cases (10.1 per cent.); cæcum, transverse colon, and large intestine, each 1 case (1.1 per cent.); and "vague," 2 cases. As is well known, the number of ulcers in typhoid fever varies considerably, and in this connection it is interesting to note that in one of these cases of perforation of the ileum the bowel presented but one ulcer, 30 cm. above the ileocæcal valve, and this solitary ulcer perforated, causing death by peritonitis.

Indeed, in recent years a large number of cases of typhoid fever entirely without ulceration has been reported. In this series there occur two such cases, and in both the bacteriology was carefully worked out, the typhoid bacillus being recovered and identified from the kidney, spleen, liver, and mesenteric lymph glands in one case, and from the kidney, spleen, and gall-bladder in the other case. This subject of typhoid fever without ulceration has been reviewed recently by Picchi, Bryant, Flexner and Harris, McPhedran and Ophüls. I have collected 26 cases, which, with the 2 cases in this series, make a total of 28 cases that seem to me to be valid on bacteriological grounds.[2] Search through the literature has yielded abundant data on the distribution of the ulcers in typhoid fever.

The material has been grouped in two divisions: first, a series of 83 individual cases, each involving unusual distribution of the ulcers; and second, a series of statistical analyses.

The 83 individual cases have been dissected below, in order to show the relative frequency of ulcerations in unusual sites:

		Cases.[3]	
Involvement of	larynx	17	
"	" pharynx	16	
"	" œsophagus	10	(4 are strictures)
"	" trachea	1	
"	" stomach	10	
"	" jejunum	3	
"	" Meckel's diverticulum	1	
"	" appendix	5	
"	" ileocæcal valve	3	
"	" cæcum	12	
"	" ascending colon	6	
"	" transverse "	5	
"	" descending "	4	
"	" sigmoid flexure	3	
"	" rectum	4	
"	" skin at anus	1	
"	" ileum and colon	12	(total 29)
"	" small and large intestine (not specific)	17	(total 29)
"	" large intestine (alone)	6	

[1] Sex: males, 66; females, 22; not given, 1. Age: twenty-one to thirty-five, 42; before twenty-one, 12; after thirty-five, 16; not given, 19 cases.

[2] Nine cases have been omitted because of a questionable bacteriology: 3 by Karlinski; 2 by Goodall; and 1 each by Banti, Thue, Guarnieri, and Dogliotti.

[3] In the appended bibliography all articles marked with an asterisk (*) contain one or more of these cases.

The general statistics from the literature have been dissected and rearranged on an anatomical basis, rather than a classification based on authorship, thus affording a more intelligible arrangement for comparative purposes. Under each anatomical division the average obtained from the data presented by the various authors is given first, followed by the result of the analysis of my series of 89 cases, and finally an average of the two totals, where both are given:

	Literature.		My series of 89 cases.	Average.
	Total cases.	Per ct.	Per ct.	Per ct.
Ulcers of mouth	.....	.....	....	none mentioned.
" larynx	1020	21.3	3.4	19.9
" trachea	439	0.2	1.1	0.38
" pharynx	648	2.5	...	2.2
" œsophagus	134	6.7	1.1	4.5
" stomach	1019	1.9	2.2	1.98
" duodenum	891	0.3	...	0.30
" jejunum	1269	6.1	1.1	5.9
" ileum	1334	89.9	75.3	89.0
" ileum (lower half)	316	37.0	35.9	36.8
" ileum (alone)	245	60.8	32.6	58.3
" Meckel's diverticulum	.....	.....	1.1	1.1
" common bile-duct	439	0.23	....	0.23
" small intestine (in any part)	534	99.4	86.5	97.5
" ileocæcal valve	.....	.....	6.7	6.7
" vermiform appendix	352	2.8	1.1	2.5
" cæcum	1307	31.3	16.9	30.3
" ascending colon	532	9.6	14.4	10.3
" transverse "	532	3.2	13.5	4.5
" descending "	532	2.1	5.6	2.6
" colon (not specific)	1092	29.1	....	29.1
" sigmoid flexure	12	33.3	3.4	6.9
" rectum	967	2.2	3.4	2.4
" large intestine	1084	22.7	50.6	33.3
" large intestine (alone)	.....	.....	5.6	5.6
No ulcers (with a bacteriology)	.....	.....	2.2	2.2

In reviewing the results obtained from a study of the literature, several facts worth noting are brought into prominence. Probably most striking among these is the wide distribution of the typhoid ulcers. They are found in every division of the alimentary tract, excepting the mouth, and they are found also in the larynx and trachea. One case has been reported by Mitchell, in which the observer speaks of a "loss of substance on each side of the tongue." No other mention of buccal involvement has been found.

Ulceration of the larynx in typhoid fever has been the occasion of much dispute, the point at issue being whether the lesion was due to typhoid bacillus or to fresh infections with pyogenic organisms (Kanthak and Drysdale, G. Duffy). Williams, in 1894, recovered the typhoid bacillus from the laryngeal ulcers in 2 cases, and since then the tendency has grown to regard these ulcers as primarily typhoidal. As long ago as 1829 Louis said: "The rarity of ulceration of the larynx is the more remarkable since ulcerations are frequently met with around that organ at the epiglottis, pharynx, and œsophagus. If laryngeal ulcers are found on a body dead of an

acute disease, they will establish with nearly perfect certainty, and without going any farther, that the affection was typhoid fever."

Ouskow has analyzed the time of appearance of the ulcers in the larynx with these results: ulcers in the first week, none; in the second week, 79 cases; in the third week, 144 cases; in the fourth week, 89 cases.

The site of the ulcers, as determined by Lüning, in a series of 165 cases, was: supraglottic in 50 cases, infraglottic in 36 cases, and in the glottis in 18 cases. The author states that the process begins in the arytenoid cartilages and extends to the cricoid cartilages.

Ulceration of the trachea, while extremely rare, occurred in 3 cases in these statistics (Ouskow, Greffier, and this series).

Pharyngeal ulcers have been noted by many observers, and I have found 32 cases.[1]

Ulceration of the œsophagus, though found repeatedly by the earlier observers, Louis, Jenner, and Chomel, later became a rarity, as is strikingly shown by Packard's review of 5000 cases, none of which showed œsophageal ulceration. To a certain extent this negative result should be regarded as due to too brief a scrutiny or complete oversight on the part of the observer, for recently Mitchell, Riesman, and Pyle have presented a total of 10 cases (4 of which were strictures with recovery) and in this series there is another case (Case I.), which is given in detail because of the unique distribution of the ulcers, they being found only in the œsophagus and colon.

Gastric ulceration, though very unusual, is now regarded as quite possible in typhoid fever and may serve to explain some cases of hæmatemesis. In one of the 2 cases of gastric ulceration in this series the entire stomach has been preserved. Sections showed the ulcers to be fairly typically typhoidal, with numerous endothelioid phagocytic cells. In addition to 20 cases found in statistics,[2] a total of 10 individual cases is presented by Chauffard, Dignat, Perignon, and Keen.

The duodenum is the second rarest site for typhoid ulcers, only 3 cases being found. Two are by Louis and the third by Andral.

The low percentage of ulcers in the jejunum, 5.9 per cent., calculated from a total of 1358 cases, confirms the general impression as to the infrequency of jejunal involvement.

Involvement of the ileum is found in 89 per cent. of the cases; of the lower half of the ileum in 36.8 per cent., and of the ileum alone in 53.3 per cent. That typhoid ulcers elsewhere than in the ileum are found more commonly than has been supposed is demonstrated by the last percentage given, especially when this is viewed in connection with the high percentage of colonic involvement about to be presented.

[1] Murchison, Moore, Osler, Ouskow, Roque, Derignac, Riesman.
[2] Murchison, Moore, Hawkins, and Andral.

Ulceration of the small intestine in any part has been recorded in 97.5 per cent. of 623 cases. Ulceration of Meckel's diverticulum has been noted twice, once in this series and once by J. Sailer.

Ulceration of the common bile-duct has been reported once by Ouskow in a series of 439 cases. This is the rarest site for typhoid ulcers. However, not only here but throughout all the statistics there is an element of doubt in the diagnoses. Perhaps it would be well to regard the ulcers as typhoidal only after recovery of the typhoid bacillus from the affected area and satisfactory demonstration of the histological picture shown by typhoid ulcers. The abrupt termination of the ulcer zone at the ileocæcal valve is well shown by the low percentage of involvement of the valve itself, 6.7 per cent.

The distribution of the ulcers in the large intestine has been considered under various captions. Involvement of the large intestine (without specification of locality) in 33.3 per cent. of 1173 cases, and of the colon in 29.1 per cent. of 1092 cases, only 65 of which are duplicates of the former number, is convincing evidence of the comparative frequency of ulceration in those sites. The division of the large intestine most frequently involved is the cæcum, 30.3 per cent. Next in order of frequency come: ascending colon, 10.3 per cent.; sigmoid flexure, 6.9 per cent.; transverse colon, 4.5 per cent.; descending colon, 2.6 per cent.; vermiform appendix, 2.5 per cent.; and rectum, 2.4 per cent.

Involvement of the large intestine alone was not found in any statistics in the literature. In this series, however, 5 cases (5.6 per cent.) were found. One of these is presented in detail (Case II.).

Chantemesse, Rendu, Hodenpyl, and Laveran describe single cases of ulceration of the large intestine alone. It may be mentioned here that Chantemesse[1] states that the typhoid ulcers may be absent throughout, except in the appendix, but he gives no details.

The distribution of the ulcers in typhoid fever having been elaborated in the foregoing statistics, the question naturally arises as to what determines this distribution, usually so typical and yet frequently so bizarre.

The answer has not yet been attained in its entirety. It is obvious that one important factor in determining the seat of the lesions is the extent and character of the lymphatic apparatus in the part. Yet the frequent occurrence of pharyngeal and laryngeal involvement, and the occurrence of such atypical cases as the two presented in this paper, indicate that accidental lodgement of the typhoid bacilli is another factor of considerable importance.

Moreover, the many authentic cases of typhoid fever without ulceration point to the existence of other possible factors, such as a lowered resistance of the gastrointestinal mucosa, which in these cases without ulcerations has reached its lowest ebb.

[1] Traité de Médecine, p. 744.

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TYPHOIDAL PERFORATION:

WITH A REPORT OF EIGHT CASES SUBJECTED TO OPERATION; TWO RECOVERIES.*

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In 1884 Leyden first suggested and Mikulicz first practised suture of a perforated typhoid ulcer. In 1885 James C. Wilson brought the subject before the profession of America, and more recently (1898) interest was aroused in this subject by the brochure of Keen. That operation is still too seldom resorted to is evident when we recall that probably over 16,000 cases perish from perforation annually in the United States,[1] and that in 1903 Harte[2] was able to collect from the literature the records of only 339 cases subjected to operation.

The mortality of typhoid fever is probably about 10 per cent., and it is said that one-third of the fatalities are due to perforation of the intestine.

Perforation usually occurs during the third, fourth, or fifth week, but may happen at any stage of the disease. Males are more frequently affected than females, and the catastrophe is more liable to take place in adolescence than in infancy or old age. When the intestinal wall becomes thinned by the process of sloughing the immediate cause of perforation may be the pressure of hardened feces, straining at stool, excessive gaseous distention of the bowel, or sudden change in posture; in a number of cases ascarides have been found in the peritoneal cavity. Perforation is usually acute and followed by marked symptoms; occasionally it is chronic and the symptoms are insidious, the peritoneal cavity being protected for some time by previous adhesions.

In approaching a case for diagnosis the age, sex, previous condition of the bowels, previous presence or absence of hemorrhage, previous severity or mildness of the disease, and the period of the

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disease may be disregarded entirely. Pain is a reliable and constant symptom, occasionally violent, usually severe, and rarely mild in character. As a rule, the pain is sudden in onset, begins in the right lower quadrant of the abdomen, quickly becomes generalized, and persists, despite the hebetude of the patient. Le Conte suggests that in view of the great sensibility of the parietal peritoneum the character of pain may be influenced by the proximity of the perforation to the abdominal wall. In a few instances the pain is reflected to the rectum and is accompanied by a frequent desire but inability to defecate. Frequency of micturition, with vesical pain, has also been noted.

Tenderness is most marked in the region of perforation, usually in the right iliac region, to which area it is limited in the beginning. Rectal or vaginal examination reveals tenderness on the right side at the onset, and later on both sides. Tenderness is of more value than pain. Rigidity of the abdominal muscles is the most valuable sign of perforation of the intestine; it is at first localized over the area of perforation, thence becoming general with the spread of infection. In uncomplicated cases of typhoid, pain is a frequent symptom; tenderness is common over the ileum, and slight rigidity may be present, but the association of these three features is an indication for exploration, and with a fair degree of accuracy indicate, by their character and extent, the intensity and area of peritonitis. The hardening of the belly-wall, due to meteorism, to emaciation, to the application of cold water, or to associated pulmonary disease, must not mislead the surgeon, who should be familiar with the feel of the abdomen in all stages of the disease.

Distention of the abdomen is often present throughout the disease, and is not an important sign, although it becomes more pronounced after perforation. The vital point is to determine whether the gas is within the bowel or in the peritoneal cavity outside the bowel. Partial absence of liver dulness may be produced by tympanitic distention of the intestine, but total obliteration of liver dulness not associated with distention of the abdomen is due to gas outside the bowel and indicates perforation of the alimentary canal. It has been suggested that in cases in which gas is free in the peritoneal cavity the chest sounds may be distinctly heard over the abdomen, but this is equally true when the intestine is distended with gas without perforation. Tschunowsky[3] claims to have heard an amphoric murmur, synchronous with respiration, over the point of perforation; he attributed the sound to the exit and entrance of air through the opening in the intestine. "In pneumatosis of the abdominal cavity one sometimes gets a peculiar quality of sound on deep percussion which resembles the cracked-pot sound."[4]

As the result of experiments on animals, Connell[5] believes that perforation may be diagnosticated by tapping the abdomen, injecting air or salt solution, and, after regaining the injected material, testing

it for hydrogen sulphide. It seems to us that exploratory incision would be more certain and less dangerous.

It has been advised in cases of suspected intestinal perforation to inject air, hydrogen, or ether into the rectum; if there be no perforation the gas will pass through the intestine and out of the mouth; if an opening into the peritoneal cavity exists the gas will pass through the perforation, increase the distention of the abdomen, and obliterate the liver dulness. This method increases the extravasation of intestinal contents and is not to be employed.

Dulness in the flanks, as indicative of fluid in the peritoneal cavity, is a fallacious sign, as it is sometimes present in the absence of perforation and often absent in cases in which perforation has occurred and in which there is a large quantity of fluid in the peritoneal cavity.

Localized impairment of resonance is of little value as a sign, as it is seldom found, even when there is an attempt at walling off the peritoneal cavity.

Immobility of the abdomen and thoracic respiration accompany rigidity, and are important signs.

Auscultation rarely reveals a friction sound, but may elicit the presence or absence of peristalsis, which is of more value from the standpoint of prognosis than of diagnosis.

Nausea and vomiting occur in less than 25 per cent. of the cases and are often present without perforation. A chill at the onset of perforation is not common. The classical symptoms of shock do not ensue as often as is generally believed. In many cases the temperature remains unchanged, and in some it rises. Sweating is a frequent symptom. The respirations are increased in frequency and thoracic in character; the pulse is accelerated and the blood pressure, as determined by the Riva Rocci sphygmomanometer, is distinctly raised.[6] The facial expression is altered and characteristic in many cases, and is a feature on which much stress is laid. A leukocytosis is only of value when corroborative of other signs.

Typhoidal perforation may be confounded with almost any other lesion producing a peritonitis, but as treatment in these cases would usually demand exploration a failure to differentiate would not be productive of harm. The most difficult differential diagnosis to make is that between intestinal hemorrhage and perforation, as the symptoms are sometimes identical and the differentiation is of the greatest importance, for to mistake hemorrhage for perforation means an unnecessary operation at a very critical period, and to mistake perforation for hemorrhage means death. The appearance of blood in the stools is not conclusive, as the two conditions may coexist. A reduction in the number of red cells and in the hæmoglobin would point toward hemorrhage, whereas an excess in the number of white cells would incline toward perforation. It is of the utmost importance to withhold opium in cases of hemorrhage

in which perforation is suspected, because of the danger of clouding the symptoms.

With Osler we may say: "That time-honored picture of perforation with the Hippocratic facies; the feeble, running pulse; the profuse sweat; the distended, motionless abdomen must be erased as not a picture of perforation, but of peritonitis, or, better still, a rough draught of death. What we need more than anything at present is a fuller knowledge of the symptoms of perforation, particularly of its onset, apart from those of the consecutive peritonitis."[7] But, unfortunately, there is nothing in the perforation itself which will enable one to suspect it; the signs and symptoms that are elicited are due to peritoneal infection, the very onset of which we should make an effort to recognize. Obliteration of liver dulness in a flat belly or resonance over the posterior and lateral area of hepatic dulness in a distended abdomen and cellular emphysema are the only pathognomonic signs of an opening into the intestine. The former, however, is a late sign, and the latter does not occur in typhoidal perforations.

The only safe rule is to have every typhoid watched most carefully, to examine thoroughly at the onset of any of the above symptoms, and to open the abdomen if the evidence gathered leave a doubt as to perforation. If there be doubt, exploration may be conducted under local anæsthesia; but if the diagnosis be positive or if exploration reveals perforation, ether should be employed, as the operation may be performed more quickly, the abdominal cavity may be cleansed more thoroughly, and the patient is not subjected to the deleterious effects of fright and struggling. Operation should be done at the earliest possible period. Some authors advise waiting for the subsidence of shock, but if shock is present the danger of delay far outweighs the danger of a rapid operation, in which the ether and the flushing of the abdominal cavity with hot salt solution tend to combat rather than aggravate the symptoms of shock. All cases should be operated upon, no matter how ill they are, as some remarkable recoveries have been reported. The incision is made in the right iliac region, as from 85 per cent. to 90 per cent. of all perforations are found in the last twenty or thirty inches of the ileum or in the cæcum or appendix. If the perforation be not found in the ileum and there are evidences of peritonitis, the sigmoid, the colon, and the remainder of the small intestine should be explored in the order mentioned, making a median incision if necessary. If the ileum be intact and there are no evidences of peritonitis, a mistake in diagnosis has probably been made, but the incision should not be closed without further exploration. Ross[8] reports a case of suspected perforation in which exploration revealed a normal peritoneum and an intact ileum; an intussusception was found in the jejunum. The perforation may be sutured with a double row of continuous Lembert sutures of silk. The

continuous suture is more rapid than the interrupted suture and just as safe. It is not necessary to excise the ulcer. A large perforation should be sutured obliquely, so as not to interfere with the fecal current. Search for a second perforation should always be made, for in 17 or 18 per cent. the openings are multiple. All suspicious spots are invaginated with a continuous silk suture. In some cases suture is impossible because of the size of the opening, because of the number of openings in a segment of the bowel, or because a piece of the bowel is gangrenous. Resection would be the ideal treatment in these cases, but as it consumes so much time surgeons have been afraid to try it. Plugging the hole with omentum or fastening the omentum over the perforation may succeed in some instances, but is a hazardous procedure. Isolating the affected portion of bowel by gauze packing has been advocated and may be employed in certain cases. The safest plan is to anchor the intestinal loop outside the abdominal cavity; this not only makes the isolation more complete, but relieves threatening symptoms of distention, and allows the local application of medicaments to the interior of the bowel for the treatment of the remaining typhoid ulcers.

After dealing with the perforation the abdomen should be flushed with gallons of hot salt solution, unless the infection be distinctly limited, in which case the affected coils should be drawn from the abdomen and thoroughly washed extraperitoneally, as a general peritoneal lavage in these cases would disseminate the infection. The abdomen is usually drained by gauze, one strip of which is pushed down into the pelvic cavity. The after-treatment is that of other abdominal cases, excepting that the patient must be carefully watched for symptoms of secondary perforation.

The prognosis is more favorable when the perforation occurs early in the disease, when the diagnosis is made quickly after the onset, and when the surgeon possesses skill and good judgment. According to Harte,[2] the mortality in 277 cases in successive intervals was as follows: 1884 to 1889, 10 cases, 90 per cent.; 1890 to 1893, 16 cases, 87.5 per cent.; 1894 to 1898, 110 cases, 74.5 per cent.; 1899 to 1902, 141 cases, 66.6 per cent.

The following is an abstract of eight cases operated upon.

Case I.—Male, aged ten years; operated upon July 28, 1901, at the Pennsylvania Hospital, twelve hours after perforation, which occurred on the thirteenth day of the disease. Pain during the entire disease, worse at the time of operation, but not severe. Tenderness all over the abdomen, but most marked in the right iliac region. No vomiting. Obliteration of liver dulness, movable dulness in the right flank, rigidity of the right rectus, thoracic breathing, distention, fall of temperature from 103° F. to normal, leukocytes 4000. Incision in the right semilunar line; liquid feces in the abdominal cavity. In the ileum, six inches from the cæcum, was a large in-

durated area, with a pinhole perforation in the centre. Double row of continuous Lembert sutures. Peritoneum injected. Death in sixty hours. Post-mortem revealed a closed perforation, the lumen of the bowel constricted one-third, and a general peritonitis.

Case II.—Female, aged twenty-three years; operated upon December 15, 1901, at the Pennsylvania Hospital, forty-eight hours after perforation, which occurred during the fifth week of the disease. This patient walked about until the time of perforation, which was inaugurated with violent pain in the region of the appendix. Admitted to the hospital immediately before operation. Vomiting, Hippocratic facies, swollen belly, obliteration of liver dulness, no dulness in the flanks, belly immobile, moderate tenderness in the right iliac region. Temperature 103° F., pulse scarcely perceptible; anæsthetic 1 per cent. cocaine solution; incision right semilunar line; large quantity of yellow fluid mixed with flakes of lymph; perforation in ileum three inches from the cæcum, one-eighth of an inch in diameter. Patient died one-half hour after operation.

Case III.—Male, aged nineteen years; operated upon August 25, 1902, at the Polyclinic Hospital during the third week of the disease, fourteen hours after perforation. Sudden severe pain, distention, tenderness and rigidity on the right side, tympanitic over liver, leukocytes 10,000. Previous diarrhœa. No vomiting, no dulness in the flanks, thoracic respiration, temperature unchanged. Perforation in ileum five inches from the cæcum, size of a lead-pencil; liquid feces in the peritoneal cavity; gauze drain through the primary incision and rubber tube through the loin. Vomited once after operation, distention less, pain absent, fever persistent, diarrhœa continued, death third day. Post-mortem revealed closed perforation, dry peritoneal cavity, and a few adhesions. Cause of death typhoid(?).

Case IV.—Male, aged twenty-three years; operated upon February 4, 1902, at the Jefferson Hospital, during the third week of the disease and twelve hours after perforation. Admitted to hospital just before operation. Pain, tenderness, and rigidity in the right iliac region. Temperature 104° F., pulse 120, respirations thoracic; severe pain, reflected to the rectum and associated with tenesmus; distention, liver dulness obliterated one-half, no dulness in the flanks, no vomiting, leukocytes 7200. Perforation in ileum six inches from the cæcum, size one-quarter of an inch; yellow feces and gas in the peritoneal cavity; gauze drain. Pulse and temperature fell to normal after operation, later rose to 103° F., and remained elevated. There were no further abdominal symptoms, but the patient died on the eighth day, apparently from typhoid. No post-mortem.

Case V.—Male, aged thirty years; operated upon June 6, 1903, at the Pennsylvania Hospital, immediately after admission. No satisfactory history could be obtained, as the patient was a Pole who understood no English. Dulness and rales over the bases of both lungs; pinched expression. Temperature 100° F., respirations

40, pulse 140, sweating; retracted, rigid belly; absence of liver dulness; costal respiration. Diagnosis perforative peritonitis; median incision; perforation in ileum eighteen inches from the cæcum, one-half inch in diameter; a smaller perforation was found one-half inch above the first perforation. Abdominal cavity filled with feces and pus. Death one hour later.

Case VI.—Male, aged forty-two years; operated upon June 7, 1903, at the Pennsylvania Hospital, immediately after admission. No history obtainable, as the patient was a Pole who could understand no English. Temperature 100° F., pulse 100, respirations 30. Great pain in the abdomen and right shoulder; tenderness all over the abdomen, and especially marked over the site of a left inguinal hernia; belly immobile and rigid, dulness in the flanks, liver dulness decreased one-half, vomitus nigra. Diagnosis perforative peritonitis; median incision; liquid feces and pus in the abdominal cavity; mesentery glands enlarged; perforation in the ileum one-half inch in diameter, three feet from the cæcum. Closure of perforation with a double row of Lembert sutures, lavage with hot salt solution, gauze drainage. Uneventful recovery. Widal reaction positive.

Case VII.—Female,* aged nine years; operated upon June 24, 1903, at the Jefferson Hospital, on the thirteenth day of the disease, three hours after perforation. The temperature had been running along at about 104° F., the pulse 120, and the respirations 20. She complained of severe pain in the right iliac region; this lasted for a short time, and the patient complained no more, even when questioned. The temperature, pulse, and respirations remained unchanged. No vomiting, slight tenderness and rigidity in the right iliac region, movable dulness in the right flank, liver dulness one finger's breadth above the costal margin, abdominal respiration. Two bowel movements between the time of perforation and operation. Tenderness on the right side per rectum, leukocytes 18,000. Incision in the right semilunar line; clear fluid in the belly, no feces or pus; peritoneum normal; perforation in ileum the size of the lead in a lead-pencil, ten inches from the cæcum and midway between the mesentery and the free border of the bowel. The perforation was closed by a small, yellowish slough, which became dislodged as the bowel was pulled through the wound. Continuous Lembert suture, flush with salt solution, and closure of the abdomen without drainage. The patient continued with the typhoid symptoms, and made a good recovery.

Case VIII.—Male, aged forty-one years; operated upon July 8, 1903, at the Jefferson Hospital, two weeks after the beginning of the

* This patient developed a small hernia at the site of incision, for which a second operation was performed four months after the suturing of the intestinal perforation. There were no adhesions in the peritoneal cavity, the mesenteric glands were still enlarged, and the site of the perforation was marked by a small grayish patch which was perfectly smooth and slightly indurated. There was no constriction of the intestine.

symptoms of typhoid and nineteen hours after perforation. The patient had been walking about up until nineteen hours before the operation, when he was seized with a sudden severe pain in the lower part of the abdomen. He was admitted to the hospital immediately before the operation. Temperature 101° F., pulse 140, respirations 30. Typical picture of a general peritonitis, liver dulness undiminished, no dulness in the flanks. Diagnosis perforative peritonitis; median incision; fecal matter and pus in the peritoneal cavity; perforation in ileum three-eighths inch in diameter, one foot from the cæcum. Death in thirty hours from peritonitis.

Analyses of cases operated upon: Sex, 6 males, 2 females. Ages nine, ten, nineteen, twenty-three, twenty-three, thirty, forty-one, and forty-two years. Day of disease on which perforation occurred: 2 on thirteenth day, 1 during second week, 2 during the third week, and 1 during the fifth week; in 2 cases no satisfactory history could be obtained, the patients being unable to understand English. Number of hours elapsing between the time of perforation and operation: three hours in 1 case (recovered), twelve hours in 2 cases, fourteen hours in 1 case, nineteen hours in 1 case, and forty-eight hours in 1 case. In 2 cases, 1 of whom recovered, the time elapsing between perforation and operation could not be determined. Pain during the entire course of the disease in 2, absence of pain previous to perforation in 4, unknown in 2. Location of pain in right iliac region in 5, general in 3. In 1 case the pain was reflected to the right shoulder, and in 1 case the pain extended to the rectum and was associated with tenesmus and a frequent desire but inability to defecate. The pain was violent in 1 case, severe in 6, and moderate in 1; in 1 case in which the pain was severe at the onset it disappeared soon after its appearance and remained absent up until the time of operation. The facial appearance was altered in all except the 2 that recovered. Mental hebetude was present in all. Previous bleeding from the bowel was absent in 6 and unknown in 2. Vomiting was absent in 5 and present in 3. Constipation had been present in 2, diarrhœa in 4, and 2 unknown. A chill was not noted in any of the 6 cases from whom a history could be obtained. In 1 case the temperature fell 3 degrees to normal, in 5 the temperature remained unchanged, and in 2 the temperature at the time of perforation could not be obtained. The pulse and respirations were accelerated in all. Localized impairment of resonance was not noted in any of the cases. Sweating was present in 6 and absent in 2. Distention was absent in 2 only. Immobility of the abdomen and thoracic respiration were present in 7 and absent in 1 case. Friction sound was not heard in any of the cases. Peristalsis was heard in 1 case, in which the bowels moved twice after perforation and in which recovery ensued. The liver dulness was totally absent in 4, partly absent in 2, and present in 2. Dulness in the flanks was present in 2 cases only. Rigidity was present in

all. Tenderness was general in 5 cases and limited to the lower right abdomen in 3. Rectal examination revealed tenderness in the 7 cases in which it was made. The leukocytes in 4 cases were 4000, 7200, 10,000, and 18,000. The diagnosis was made in 5 cases, and the incision was made in the right iliac region; in 3 cases a diagnosis of perforative peritonitis was made and the abdomen opened in the middle line. The perforations were situated in the ileum within three feet of the cæcum in all cases, and varied in size from a pinhole up to one-half inch in diameter. In 1 case there were two perforations. Fecal matter was present in the peritoneal cavity in all except 1 case, in which the fluid was clear and in which recovery ensued. The peritoneum was inflamed in all but 1 case, in which recovery ensued. Mesenteric glands were enlarged in all. In only 1 case was it necessary to tear through adhesions to find the perforation. In all cases a double row of continuous Lembert suture of silk was employed. All were drained with gauze, surrounded by a rubber dam, except 1 (recovered); in 1 case (died) in addition to the gauze drainage in the primary incision a rubber tube was brought out through the loin. Ether was used as an anæsthetic in all cases except 1, in which the operation was performed under cocaine. 5 of the cases were admitted to the hospital immediately before operation, and 2 walked about until the time of perforation. 2 recovered, 2 died of typhoid (?), and 4 died of peritonitis.

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PAROTITIS COMPLICATING APPENDICITIS.[1]

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THE first reported instance of parotitis as a postoperative complication of appendectomy is that reported by Barlow, in 1886, who, in a male aged twenty years, reports the occurrence of a parotid bubo, "which did not suppurate." In the operation, collections of fetid pus around the cæcum had been found. The appendix vermiformis was noted to have been much thickened, but apparently it was not re-

[1] Read before the Academy of Medicine of Toledo, Ohio, October 23, 1903.

moved. Elder and Thomas next, as recently as 1901, each mentions the occurrence of parotitis as a sequel to appendicitis. In Elder's case, a male aged twenty years had a sudden onset of pain in the right iliac region. The operation revealed pericæcal abscess. Three days after the operation the temperature began to rise, and a stiffness and swelling in the right parotid region, with intense pain, appeared. "The swelling rapidly increased for about ten hours, when the pain subsided. At this time the whole parotid region and the upper part of the neck were enormously swollen, the swelling coming forward over the cheek and involving the eyelids, especially the under one. Thirty-six hours after the left parotid began to swell in the same way, while the right parotid began slowly to decrease. The left parotid attained almost exactly the same size as the right, and the temperature reached 103° F. The swellings were very painful to pressure, but there was no indication of suppuration in either of them. The second parotid reached its maximum in about twelve hours after it showed symptoms of enlarging." Both parotids gradually subsided, and recovery followed. As a probable etiological cause in this instance, infection is suggested.

In Thomas' case, that of a young woman aged twenty-two years, the appendix was found adherent to the pelvic bottom, but no suppuration was present. Six days after the operation a parotitis developed on the right side, which was extremely painful and persisted for ten days, then subsiding without suppuration.

In these three instances of postoperative parotitis following appendectomy are to be found the only records of this complication subsequent to this operation. As noted, in two, suppuration occurred, while in one of these a septic condition was presumably not present. To these three cases I wish to add three others which have come under my own observation.

Case I.—Male, aged twenty-nine years, entered Charity Hospital May 12, 1902, with severe attack of appendicitis. Patient refused operation, and a large mass formed in the right side. All food was withheld from the stomach, and feeding was carried on exclusively by the rectum. In about seven days, when the general symptoms were improving, though the tongue remained dry and hard, he developed a tenderness over the right parotid. Ichthyol and hot fomentations were applied, suppuration occurred, and the abscess was opened May 24th. The left parotid up to this time had not been involved, but in a few days became inflamed, suppurated, and was opened May 28th. The pus was at first very thick and white, but later it became thin, the drainage was better, and they slowly healed. The mass entirely disappeared, and the patient was discharged June 27th, entirely recovered. He was seen at the expiration of one year and had had no recurrence of the trouble.

Case II.—Male, aged twenty-nine years, entered Charity Hospital January 28, 1903, with an attack of acute appendicitis, this

being the fifth attack within the past year. At this time the patient had a mass in the right side, and vomited severely, apparently obstruction of the bowels. Immediate operation revealed abscess cavity and gangrenous appendix, peritoneal cavity well walled off. Appendix was removed and wound drained. No movement of the bowels was obtained until the second day. He suffered from great pain and extreme distention of the abdomen, and was allowed nothing by mouth but hot water and occasionally a little beef broth. About February 6th he developed a right parotitis, which slowly went on to suppuration, and was opened. In two or three days the left parotid became involved, and though greatly swollen and very painful, never had to be opened, but was treated with local applications of ichthyol and moist heat. The bacteriological examination showed a pure culture of bacillus coli communis from the appendiceal abscess and staphylococcus pyogenes aureus from the parotid abscess. Patient discharged cured March 25th. At no time did the parotid inflammation appear to threaten the life of the patient, and in the one which suppurated, recovery followed fairly rapidly upon its evacuation.

Case III.—Female, aged sixty-two years, admitted to Mt. Sinai Hospital July 16, 1903, had been sick for one week, suffering intense pain in abdomen, especially in the right iliac region, had severe diarrhœa, brought on by purging, vomited frequently, abdomen markedly distended, large mass in the right iliac region. Diagnosis, appendicitis. No operation was performed; patient was allowed only water by the mouth, and was fed by the rectum, and ice-bags applied to the abdomen. Under this treatment the fever gradually declined until July 22d, when it reached normal, and remained, with slight variation, at that point till July 26th, when it rose to 100.4° F. Coincidently there was a beginning tenderness of the left parotid, which increased greatly in size, the swelling extending back of the ear and well down on the neck. On account of the pain and swelling she could only separate her jaws about one-quarter of an inch. The tongue was very dry and hard. Five days later, under local anæsthesia, the parotid was opened and a small amount of very thick pus escaped. The pus was so thick that for several days the flow was much impeded. By July 30th the temperature was again normal, but August 2d it rose to 100° F., and a beginning parotitis of the right side was discovered. This was treated as was the first, by local applications of ichthyol and hot fomentations. The tongue remained dry and harsh, the jaws almost entirely closed, but the inflammation gradually subsided without evidence of suppuration, and the patient's general condition improved very markedly till August 9th, when she complained of some pain and discomfort in the right iliac region. The mass had disappeared after a week's confinement to rectal feeding, and was not again present, but the temperature rose to 101.4 F., and then gradually resumed the normal, remaining there

for several days prior to her death on August 21st. No autopsy was permitted, so that the exact cause of death was not known. Both parotids had, however, entirely recovered. There was no evidence of metastatic processes, but the condition seemed to be rather one of low sepsis and exhaustion.

The records of these cases, especially the bacteriological findings, are unfortunately incomplete, but in the second case, or the only one in which an operation was performed and an opportunity given to compare the bacteriological cause of the appendicitis and also of the parotitis, the examination showed colon bacilli in the one and staphylococci in the other, thus showing the improbability of its being metastatic in its origin, and in all three cases both parotids became entirely well and no metastasis developed, and aside from the additional debility or exhaustion which ensued, the parotitis did not seem to be *per se* a serious complication.

Since the completion of this paper the following report of a case of parotitis complicating appendicitis has been kindly given me by my colleague, Dr. C. A. Hamann:

E. R., aged twenty years; operation on November 23, 1901. Three weeks before operation was attacked with usual symptoms of acute appendicitis. Condition at time of operation: Large tender mass in median line of abdomen, below and to left of the umbilicus, plainly to be felt per rectum; fluctuation not to be determined, temperature, 101° F.; pulse, 92; leukocytosis, 27,000. Incision in median line. Abscess cavity contained about one pint of pus, walled off. Pus had a fecal odor. Bacillus coli communis found. Appendix could not be found. On November 28th the left parotid region was greatly swollen; œdema over gland; pain; temperature, 102° F. November 29th, incision; no pus evacuated. December 4th, another incision; much pus; About this time the right parotid became enlarged. Soon pus appeared in the external auditory canal. December 7th, incised right parotid; much pus; bacillus coli communis and staphylococci found in pus from parotids. Patient progressed gradually to complete recovery. Discharged from the hospital January 4, 1902.

It will be noted that in this case the colon bacillus, as well as staphylococci, were found in the examination of the pus obtained from the parotid, but no other evidence of metastatic infection appeared, and the patient eventually made a favorable recovery.

The occurrence of parotitis as a sequel or complication of various operations and diseases, though known and described by many clinicians, is still of interest and of importance, and while the object of this paper is to emphasize the possibility of its occurrence in appendicitis, it is also my desire to refer as briefly as possible to a number of cases which have been from time to time reported and the theories which have been advanced to account for them.

Parotitis as occurring subsequent to abdominal sections has been

most frequently noted in relation to ovariotomy. Goodell, in a series of 153 ovariotomies, noted its occurrence in 4 cases, in only 1 of which did suppuration occur. Moricke, in 200 ovariotomies, observed 5 cases, 4 of which suppurated. Paget, in a collection of 101 cases of parotitis, the result of injury, either traumatic or operative, to the abdomen or pelvis, reports that in 27 it was the sequel to ovariotomy or oöphorectomy. In 90 of these cases both parotids were attacked, and in 3 the submaxillary and sublingual glands were also involved. Brunne, in a report of 17 cases of parotitis supervening upon ovariotomy, reports that in 4 cases it was bilateral, while in 9 cases suppuration occurred.

From this great preponderance of parotitis subsequent to ovariotomy it was at one time assumed that it occurred only in this operation to the exclusion of all others. Moricke asserted that he had never observed this complication in any other laparotomy excepting that involving an ovariotomy. This statement was, however, soon contradicted by more accurate observations, and other operations followed by this complication were soon reported.

According to McDonald, parotitis was not an unusual or uncommon complication in the early history of abdominal surgery, it being regarded by some surgeons as invariably fatal. This statement regarding the fatality of postoperative parotitis was seemingly substantiated by Moricke, who also regarded the parotitis following ovariotomy as a severe complication, stating that in 2 cases it was seemingly the sole cause of death, and in 2 cases it at least contributed to the fatal issue.

As to the etiology of postoperative parotitis, the theory which was primarily advanced assumed the sympathetic relation between the generative organs and these glands. This theory, which gained some corroboration from the frequent occurrence of orchitis or mastitis following the so-termed mumps of childhood, was apparently even more strongly verified by some peculiar instances of parotitis following injuries or operations on these organs.

In the male sex parotitis had been observed secondary to injury of the testicle (Billroth, Hutchison), after the passage of the catheter (O'Conner, Crimm, Paget), as also subsequent to cystitis (Paget). In the female sex, however, parotitis had been even more frequently observed in the various affections of the generative organs. Peter, in a woman with irregular menstruation, speaks of the substitution of the menses by parotitis of either one side or the other, most frequently the left. Hawkins mentions the instance of a woman who, during six successive pregnancies, had an enlargement of the left parotid, which increased with the advance of gestation, and totally disappeared after delivery. He states that "she had learned to recognize this as one of the first indications of her condition." Cribb, in connection with the interrelation of parotitis and the sexual organs, speaks of an instance in which parotitis followed the insertion of a

pessary in the vagina. Parotitis following delivery, abortion, and the menopause, has also been mentioned by other observers, also as a sequence to operative procedures on the generative tract, as has been observed after the excision of the cervix, uterus (Goodell), the repair of a lacerated cervix (Emmet), the repair of a vesicovaginal fistula (Emmet), abdominal hysterectomy (Krussen, Ross, Baldwin, McDonald), salpingectomy (Ricketts), perineorrhaphy (Auld), myoenucleation of the uterus (Gotschauer).

In the frequent observance of parotitis as resulting from disease, injuries, or operations upon the sexual organs, the sympathetic bond between these respective organs seemed assured, even although a more or less direct anatomical connection could not be determined. Trousseau already referred to it in a vague manner. Brunn advanced the explanation that stimuli were transferred from one organ to the other by means of certain nerve channels. In this way irritation in operations on the ovary was said to cause vasomotor disturbances in the parotid gland, from which an inflammation soon followed, which at the onset was assumed to be simple. If suppuration subsequently occurred, this was supposed to be the result of microorganisms, whose portal of entrance was through Stenson's duct, the partial suspension or inhibition of the salivary secretion being considered a most favorable and influential factor for the admission of the micro-organism.

Paget similarly assumed a nervous relation, although he, too, could advance no more definite statement as to the nature of the relation. The assumption of Paget was largely based on instances of persistent alteration of the parotid gland of both a physiological and clinical nature. In the dog, for instance, the action of the gustatory nerve is known to suffer inhibition when a loop of intestine is drawn from the abdominal cavity, and the secretion of saliva is thereby diminished or totally arrested until the loop of the intestine is replaced. Clinically, he states, arrest of saliva has also been observed during gastritis, as also during menstruation, while in pregnancy salivation is a common occurrence.

This influence of the nervous system on the salivary glands is said to be both direct and reflex. In all of these assumptions a clear elucidation of the exact anatomical and physiological interrelationship of these organs to either the nervous system or to the parotid gland seemed lacking, so that they presented but little which could logically commend itself. With more accurate observations on this form of parotitis it was also found that the affection was not entirely limited to operations upon the sexual tract, but occurred after other cœliotomies and operations. In the report of such instances it had been noted as a sequel to gastrectomy (Clark), gastrostomy (Paget), enterostomy (Dunkworth), colostomy (Dashwood, Rosenbach), laparotomy for peritonitis (Goode, Addenbrook), partial removal of the omentum and retroperitoneal tumor (Paget), operation for

gastric ulcer (Hawkins and Herbert), as well as after a division of a rectal stricture and excision of hemorrhoids (Paget, Auld), and after an amputation of the leg (McDonald), so that the statement that parotitis following operation is confined exclusively to operations upon the generative tract is no longer valid, and the theories which had been advanced were changed to include all interference upon the peritoneal cavity. A definite relation identical to that which had been theoretically applied to the ovaries was, however, assumed to exist between the peritoneum and the parotid gland.

In this connection Brunn mentioned that in the cases of parotitis following ovariotomy which he had observed this seemed to be most frequent when multiple adhesions between the viscera were encountered. To explain the occurrence of parotitis subsequent to laparotomy or operative interference in the peritoneal cavity in general, a new theory, however, soon came in, viz., that of direct metastasis. As has been frequently stated, parotitis was more apt to result if purulent foci were encountered in the course of the operation subsequent to peritonitis, pyæmia, appendicular abscess, etc., than after non-septic cœliotomies.

Pozzi regarded the occurrence of parotitis after cœliotomy as strong evidence of the fact that a certain degree of septicæmia was present. In general, however, the theory of metastasis where no purulent affections and septicæmic processes were present could not be regarded favorably. Among later writers this theory too has been discarded, as it could not logically be assumed that septic metastasis should involve the parotid gland to the exclusion of all other organs. The more rational view that parotitis was to be associated with an ascending infection from the mouth along Stenson's duct began to prevail, and the clinical facts, when carefully considered, in part if not wholly, served to substantiate this view. Certain predisposing factors favoring the ascending infection along the course of Stenson's duct were soon determined to be present in the instances in which parotitis supervened. Among the most influential of these is the dryness of the mouth, which may supervene after operations and in conditions of enjoined rest of the patient. Contributory causes are the stagnation of the saliva and the injury to the duct in the course of the operation. That dryness of the mouth predisposes to a parotitis has been attested by clinical observations of various writers.

In the affection termed erostomia the occurrence of repeated attacks of parotitis has not been infrequently noted (Hutchison, Harris, and Battle). Gee, in the consideration of the inflammation of the parotid as complicating the various fevers, regards it as being caused by the dryness of the mouth, the irritation being assumed to extend from the mouth along Stenson's duct to the gland. Next to the dryness of the mouth the stagnation of the saliva may be said to constitute the most favorable factor for an ascending infection along Stenson's duct.

The conditions under which a patient is placed subsequent to the operation may well be considered as powerful contributory factors in the causation of parotitis. The feverish condition often following operations, by reducing the quantity of secretion, leads to a still further stagnation of the saliva within the glands and ducts. The failure to clean the teeth in the first few days following the operation may also act as a contributory cause. Thus in 2 cases reported by Malcolm the opening of Stenson's duct was visibly inflamed when attention was first directed to the gland, and in both cases carious teeth were situated opposite the opening of Stenson's duct. Hawthorne noted this early infection of the duct, stating that from the very earliest appearance of parotitis, pressure over the duct would cause the expulsion of a drop of pus from its orifice.

The histological investigation of Hannau in several fatal cases complicated by parotitis also bears out this view that an ascending infection from the mouth is the primary and direct cause of this affection. Paget at once refuted this theory, advancing as the most patent argument against it that the socia parotidis were never inflamed before the main body of the gland. This objection seems, however, not to be of great value, as clinically it must be difficult to establish an inflammation of such a small portion of the gland. Its attendant enlargement can be but slight, and the pain upon palpation cannot probably be so accurately localized as to enable us to say whether it is in this part or the anterior portion of the gland proper. Moreover, as has been determined histologically and clinically, inflammation of Stenson's duct precedes that of the parotid gland, so that the refutation of Paget may be considered as resting on insufficient or faulty observations.

One of the possible contributory causes not heretofore mentioned is the injury to the gland or duct, which may occur during the administration of anæsthesia. In the various manipulations of the face, as in the forward action of the mandible, the traction of the tongue or the removal of the accumulated secretion of the mouth, the duct may be easily compressed. A somewhat severe compression might at times result in slight injury, such as contusion of Stenson's duct, a locus minoris resistentiæ be thereby established, which, either singly or in conjunction with the dryness of the mouth and stagnation of saliva, would prepare a favorable field for a parotid infection. Occlusion of the duct at its most constricted portion, the papilla, which is situated opposite to the second upper molar tooth, would, similarly, be at times the result of this manipulation in the course of the anæsthesia. That these injuries of the duct favor the development of a parotitis is maintained in the cases reported by Johnson, in which the only cause that could be ascertained was an inflammation of the duct, with stagnation of the salivary secretion. Similar cases have been reported by Choppell, Battle, Kussmaul, and others. In several of these cases it was noted that pressure over the duct or

gland relieved the swelling, and it was found that the pressure caused the expulsion of a plug of thick, turbid mucus from the duct, thus relieving the obstruction to the escape of saliva.

The various theories which have been advanced to explain the occurrence of postoperative parotitis may be stated as follows:

1. A sympathetic or nervous connection between certain viscera, notably the ovary and the parotid gland.
2. Metastasis.
3. Direct infection of the gland by way of Stenson's duct.

The theory of a sympathetic relation is not only entirely hypothetical, but extremely improbable. It is based for the greater part on a collection of facts having little apparent relation to each other, except that in all the parotid gland is involved, and there seems to be no relation other than that indefinite one termed reflex, which may not only take place after operations and injuries of various organs, but as the result of psychical emotions. Similar or identical reflex disturbances are also encountered in other gland structures, and are not, therefore, confined to the parotids. It is known, for instance, that in the emotion of fear the secretion of the parotid gland is inhibited, and in surgical shock also the flow of saliva is in part arrested. In neither of these, however, is the parotid gland alone involved. If shock is of any duration all glandular structures are said to be similarly involved. The increased salivation of pregnancy cannot be directly attributed to the uterus. It is more likely the consequence of the general condition. The statement that in camels the parotid glands enlarge during the breeding season may be included under this explanation. The functional alterations in the parotid secretions after operations, if it occur, is of temporary duration, so that it is doubtful whether as such it could favor inflammation.

The clinical observations of the occurrence of orchitis following mumps might possibly be explained by the theory that the causative agent was transferred accidentally by the hand from the mouth to the urethera, thence to the vas deferens, and finally involving the testicle. The occurrence of parotitis following catheterization attended by pain and fear might be due to the psychical effect which temporarily inhibited the secretion of saliva, and thus favored infection, but it could scarcely be more than a contributing agent, and, therefore, the role of sympathy in the production of inflammation of the parotid should be excluded.

That metastasis may and sometimes does occur in the parotid gland cannot be denied, especially in pyæmic or septicæmic cases, but it seems hardly probable that the parotid alone should be involved, while all the other organs of the body and more frequent sites of metastatic deposits should escape. So that while in single instances this metastasis may be assumed to have occurred, we cannot insist upon this being the universal or even common cause.

Direct infection, in the light of modern pathology and from the

clinical study of many cases, would seem to be the only tenable theory, and while no doubt a large percentage of these infections occur primarily in Stenson's duct, the known fact that many pathogenic bacteria are cast off through the salivary glands make it not improbable that the locus minoris resistentiæ having been prepared by the dryness of the mouth, the stagnation of saliva, the inactivity of the masticatory muscles from the enforced liquid diet, or from possible injury to the duct or gland in operation, the bacteria may develop directly in the parotid, even while the duct is the site of an inflammation derived from bacteria within the buccal cavity.

PROGNOSIS. So far as may be judged from the few reported cases of parotitis following appendicitis, this complication is not to be considered a serious one or one likely to lead to any grave results, obviously very different from those rare cases of pyæmia, with coincident involvement of the parotid.

TREATMENT. The treatment must be regarded as (1) prophylactic and (2) surgical. The prophylactic treatment consists in attention to the buccal cavity, frequent cleansing of the teeth, washing out the mouth with a mild antiseptic, such as boric-acid solution, freeing the tongue so far as possible from the foul deposit which so often accumulates upon it, and in the cases in which stomach-feeding has been interdicted, giving the patient something to chew, so as to bring into action the masticatory muscles, and not only help in this manner to evacuate Stenson's duct of the accumulated mucus, but in a mild way stimulate the salivary secretion. Where not objectionable to the patient, chewing-gum might prove the most suitable agent. It might be proper, again, to call attention to the possibility of injuring the duct or gland by external manipulation, especially during the administration of an anæsthetic.

The surgical treatment consists in the application of heat or cold in the hope of checking the inflammation, but where pus is obviously present, nothing remains but to evacuate and drain, and a satisfactory recovery may be confidently anticipated.

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NASAL SYPHILITIC TUMORS.

By Max Toeplitz, M.D.,
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The tertiary manifestations of syphilis, in the nose the most frequent, are often seen very early—a few months to one year after the first infection, but, as a rule, much later. The tertiary lesions of hereditary lues are the same as those of the acquired, and occur either soon after birth or during puberty.

The anatomical lesion is a gummous infiltration of the mucous membrane, independent affection of cartilage, periosteum and bone, and simple infiltration, with softening, ulceration, either from without inward or inversely. The favorite seat of the infiltration is the septum, particularly on the boundary line between the quadrilateral cartilage and the perpendicular lamina of the ethmoid, bilaterally, often as the only sign; but it also occurs on other places of the septum, rarely on the lateral nasal wall, the turbinates first, but most frequently on the septum and nasal floor.

The tumors are either extremely large gummata or so-called granulomata. Such a syphiloma occurred in a woman, aged twenty-six years, an inmate of the Montefiore Home, who suffered from obstruction of the left nostril, formation of thick crusts, loss of sense of smell, and severe epistaxis. In the right nostril the most anterior portion of the lower turbinate covered with fibrinous deposits was seen only, owing to a deviation of the septum. The left nostril was obstructed by a gray, reddish, movable, smooth tumor, which was removed piecemeal with the cold snare, with much hemorrhage. It sprang from the upper portion of the bony septum, viz., from the upper raised boundary of a perforation, through which the tumor disappeared into the right nostril. The interior of the nose was covered with thick, foul-smelling, green-gray, adhesive crusts. The middle turbinate was atrophied. The histological examination, made by Dr. Henry Kreuder, revealed the body of the growth to consist of loose fibrous connective tissue covered in places by epithelium of the stratified columnar variety. The epithelium dipped

down into the tumor and formed small retention cysts, which were lined with stratified columnar epithelium and were filled with mucus. Throughout the connective tissue many large bloodvessels with thin walls were seen and areas of inflammatory round-celled infiltration. Besides, there were areas of larger cells, almost round, with large nuclei, which were suspicious of sarcoma. When the patient entered the Home, on June 20, 1902, she was considered tubercular. Bacilli resembling tubercle bacilli were twice found in the urine. She was removed to the tubercular ward, but as the sputum was always negative she was transferred to another ward. Iodide of potassium was first given on March 3, 1903, in doses of 20 gr., t. i. d., which were increased to 50 gr., and continued till September 20, 1903. Two courses of mercury rubbings, each lasting six weeks, were applied between April 1st and July 23, 1903. Iodide of potassium (10 gr.) and Fowler's solution (3 minims), t. i. d., were given for one month. On February 1, 1904, began hypodermic injections of bichloride of mercury, $\frac{1}{10}$ gr. daily. The antisyphilitic treatment was continued for other than nasal lesions; an annular stricture of the rectum, causing obstruction, which was relieved by cutting through the ring, but along which a syphilitic neoplasm still remained.

An analogous case is reported by Kuhn, in which a mother of four healthy children presented in the vestibule of the left nostril a soft, slightly bleeding tumor, the size of a walnut, covered with smeary pus, and connected, through a perforation the size of a quarter in the cartilaginous septum, with a similar, somewhat smaller tumor in the right nostril, both of which obstructed the nasal cavities completely. Microscopically the tumor consisted of cellular tissue of moderate vascularity, mostly round cells and young connective-tissue cells. Besides, it contained a large number of partly rounded, partly elongated giant cells, with numerous processes and marginal nuclei, and at some places firmer tracts of connective tissue.

Another such case with perforation of the septum is given by Kuttner, who holds that a gummous growth originating from the periosteum had broken down, causing a carious destruction of the septum. The syphiloma or granulation tumor had grown alongside of it. Another explanation is this: The decay of the gumma produced an inflammatory irritation of the surrounding tissue, giving rise to granulation.

These tumors obstruct the nose when large enough, and discharge fibrinous, smeary, and purulent secretions. They cause pain in the head, face, shoulder, and paralytic-like weakness in the arm. They are of variable size, and are implanted upon the mucous membrane with a broad or pedunculated base. Their favorite seat is the anterior lower portion of the septum, occasionally, also, the nasal floor. They are red, reddish-gray, not quite smooth, show frequent erosions, but rarely ulcerations. They are covered with fibrinous, purulent, firmly adherent exudations, in some cases with thin, fluid,

mucopurulent secretion. The tissue is boggy, brittle, still without tendency to decay, its main distinction from gumma.

Von Esmarch has warned against superfluous and harmful operations which are carried out for these syphilitic tumors when their nature is not recognized.

In Knight's case the appearance of manifest specific signs prevented the operation. A girl, aged fifteen years, had suffered from epiphora through a stenosis of the nasal duct due to an enormous enlargement of the right inferior turbinated body, which blocked up the nostril completely and was adherent to the septum. The mass was removed, but in two weeks had resumed its original proportions. Another recurrence took place after removal, and microscopically a small round-celled sarcoma was diagnosed. A general surgeon advised excision of the upper jaw. Ten days later a sensitive swelling of the left chin and a semifluctuating tumor of the size of a hen's egg appeared over the crest of the tibia. Under mercury and iodide of potassium in rapidly increasing doses the tumors of the nose, chin, and tibia disappeared within two weeks.

Many such histories could be related in which the microscopic examination revealed apparently a sarcoma, which disappeared under antisyphilitic treatment.

In several of Kuhn's cases the tumor was due to direct infection, while in a girl, aged eight years, numerous syphilomata had appeared in the nose as late manifestations of congenital syphilis.

I have seen a number of cases of multiple tumors under and along the lower turbinate which resembled a papillomatous growth and recurred as rapidly as they were removed, but were cured with mercury and iodide of potassium.

Theisen reports three cases: The first in a child, aged seven years, with tumors of the septum, of the size of small cherries, pedunculated, like papilloma, which contained spindle cells, recurred after removal and disappeared under iodide of potassium. The second case in a man, aged thirty-six years, was a tumor, of the size of a walnut, and was attached to the septum. It contained tubercle bacilli and giant cells. The third case was a large tumor in a man, aged fifty-eight years, springing from the inferior turbinate, which also showed a swelling of the right cheek.

The diagnosis of these tumors is difficult if the patients do not exhibit other syphilitic signs and the history does not furnish any support. Microscopic examination does not give any positive results as to the specific nature.

The new formations are true tumors, pure connective-tissue growths originating from the submucous connective tissue. The giant cells, which resemble the tuberculous giant cells of Langhans, are proliferations of endothelia from the walls of small veins, and the leukocytes also take part in their production.

The fibrous connective-tissue stroma is the distinguishing feature between these tumors and the round-celled and spindle-celled sarcoma, in which the fundamental substance is sparse and more homogeneous or slightly granular.

The granulomata or syphilomata are not to be confounded with the frequently occurring nasal gummata, which are an inflammatory infiltration into the mucous membrane along its prominent surface, and which soon decay and ulcerate. The syphilomata, however, originate from a small circumscribed place of the mucous membrane, develop to a considerable size, and do not exhibit any tendency to decay.

The clinical proofs are the history and other syphilitic lesions. Perforations of the nasal septum are not always specific; they may be due to congenital or developmental influences, traumatic (operations), contiguous pathological conditions, and influences engendered by constitutional diseases, local inflammations, and allied processes. I have found the greater majority of workingmen in a Paris green factory with perforations of the nasal cartilaginous septum.

The best criterion for the diagnosis is the success of the antisyphilitic treatment. Kuttner had in one case given iodide of potassium without success, and, therefore, had considered the growth as non-specific, but when he later combined it with mercury he succeeded in curing the case.

The antisyphilitic treatment shows the best results with nasal syphilomata.

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ICTERUS IN SECONDARY SYPHILIS.

By W. J. Calvert, M.D.,
missouri state university.

C. D., aged twenty-seven years, male, American, white, was admitted to the Post Hospital, Fort McHenry, Md., on June 6, 1902, with intense jaundice. Family history was negative; personal history includes ordinary diseases of childhood; no recent sickness.

Present illness began six weeks ago, when a hard chancre developed on the right side of the glans penis. About three days ago, June 3, patient thinks he had a very slight fever (doubtful), when he also noticed his jaundiced condition. All duties pertaining to his profession were performed until the day previous to entering the hospital. Physical examination on admission revealed an intense general icterus; hard, indurated chancre with one enlarged, hard, right inguinal gland; slight general glandular enlargement; no fever; no pain; no skin lesions; thorax and abdomen negative. Liver was normal in size and not sensitive to pressure. Urine showed bile pigments, no albumin. Feces were not totally decolorized. Three days after admission the first appearance of a general macular eruption was noted.

On admission calomel and soda were given and patient put on bichloride $\frac{1}{16}$ grain and potassium iodide 10 grains t. i. d. On January 25th all secondary symptoms and jaundice had disappeared and patient was discharged from the hospital with the usual instructions.

During his stay in hospital no fever or digestive disturbances were noted, appetite and general condition good. Patient at no time complained of pain. Diagnosis was icterus associated with secondary syphilis.

While icterus in secondary syphilis has long been known, the literature on this subject is comparatively limited.

Extracts from literature: Paracelsus, in 1510, speaks of icterus associated with syphilis, and in 1555 noted the frequency of liver affections in hereditary syphilis. In 1740 Astuc pointed out that icterus followed obstruction and congestion of the liver, as was later mentioned by von Swieten, in 1743, and Fabre, in 1765. Rosen de Rosenstein, in 1764, admitted the co-existence of icterus and syphilis, but thought the icterus was due to the mercurial treatment. Portal, in 1812, admits that icterus is associated with secondary and tertiary syphilis. Guebler, in 1852, reported 5 cases; and Luton, in 1856, first pointed out the difference between icterus in secondary syphilis and that in catarrhal conditions. Three cases were reported, in 1864, by Lancereaux. Lacombe, in 1874, and Morelard, in 1879, report new cases; while Schroeder, in 1887, reported 7 cases. Engel-Reimers, 1887, recorded a case of acute yellow atrophy in secondary syphilis terminating fatally. More recently, Lasch, in 1894, reported 3 of his cases and 46 from the literature; Neumann, in 1895, records 14 cases; Lowenstein, 1. From the records in Allgemeinen Krankenhause in Hamburg, Werner reports 57 new cases of icterus in secondary syphilis out of a total of 15,799 cases, or 0.37 per cent. Aschner, in 1896, reports 3 cases; and Jaumenne, in 1899, 2 cases.

It is difficult to ascertain the exact number of cases as the literature at my disposal often says that some new cases were reported.

Starting with Lasch, who reports 46 cases from literature and 3 of his own, we have, Neumann 14, Lowenstein 1, Werner, 57, Aschner 3, Jaumenne 2, Calvert 1, or a total of 127.

Naturally the etiology of this manifestation is obscure, consequently it has given rise to numerous speculations, no one of which covers all the cases.

Lancereaux, Engel-Reimers, Quincke, and others think the icterus is caused by enlarged glands pressing on the bile-ducts.

Senator, Hutchinson, and Chapotot agree with Guebler, who thinks the secondary eruptions in the intestines cause an obstruction in the flow of bile.

Maurice thinks the hyperæmia of the bile capillaries, due to inflammation of the liver, is sufficient cause. Schroeder believes general catarrhal condition, similar to the infectious diseases, exists. While Quadillac holds that the changes in the blood due to syphilis produce icterus. Several French writers think the general condition of the nervous system plays a role; so use the term "jaunisse émotive," while others use "meta-syphilitique."

Neumann considers changes in the vessels a sufficient cause; Eichhorst and others favor the chemicotoxic theory;. and Liebermeister advocates Menkowsky's idea of acatactic or diffusions icterus.

It is perhaps safe to say that one or more of these causes may be present in the same case. Two types occur—benign and grave.

In benign cases icterus develops rapidly without the usual digestive symptoms of catarrhal jaundice, as was first pointed out by Luton. In 75 per cent. of the cases jaundice develops simultaneously with the secondary symptoms; in the remaining percentage of cases either before or after the onset of secondary manifestations. The character of the secondary lesions is unimportant. In degree, the jaundice varies from a light tinge to a deep discoloration. Its course runs parallel with the secondary symptoms and, like them, may recur. In duration icterus exists from a few days to two months, and if treatment is neglected may become chronic. Occasionally, varying degrees of sensitiveness is present in the hypochondriac regions. Two of Werner's cases presented enlarged livers. Spleen is normal in size. Urine shows ordinary findings. Feces more or less decolorized. Pruritus seldom. Werner noted xanthopsia three times.

In the grave cases icterus develops as above recorded, but on the fifth or sixth day, delirium, hemorrhage, purpura, or coma, often followed by death, may develop in a remarkably short time.

The diagnosis of this manifestation is usually easy. There is a history and evident signs of syphilis. The secondary eruption may be present when the patient is first examined. The following points are most distinctive:

1. Appears in secondary stages of syphilis.

2. Simultaneous appearance with secondary lesions.
3. Influenced by specific treatment.
4. May vary in degree as the secondary eruption varies in intensity during the course of the disease, and, like the eruptions, may recur.
5. Rapid appearance without digestive disturbances.

Even the grave cases if properly treated are rarely fatal. Treatment consists in ordinary treatment for syphilis in this stage.

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Index Catalogue of the Library of the Surgeon-General's Office.

BRIEF REPORT OF A CASE OF SPRING CONJUNCTIVITIS RESEMBLING MALIGNANT GROWTH OF THE CORNEAL LIMBUS.[1]

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EARLY in October, 1902, H. H., a male, aged twenty-four years, native of Virginia, was brought to me by one of my clinic assistants for the purpose of having a growth removed from the corneal limbus of the right eye. This growth had been observed first about two years before as a small elevation 2 mm. to the temporal side of the limbus in the centre of a small, circumscribed patch of conjunctival injection, and had increased in size until at the time of my examination it was 5 mm. by 7 mm. in breadth and encroaching upon the cornea. It presented an angry, bluish-red appearance, and, though apparently situated in the conjunctiva, was firmly adherent to the underlying episcleral tissue. The patient complained of the disfiguring appearance, sensation of a foreign body, slight burning, and some conjunctival discharge. Further examination of the eyes and lids revealed nothing abnormal, excepting a moderate refractive error, and the patient was confident that the condition had been uninfluenced by the seasons and that the growth had been gradually increasing in size for two years. No family history of tumors of any kind could be obtained.

[1] Read before the Section on Ophthalmology of the College of Physicians of Philadelphia, March 15, 1904.

The growth was excised under cocaine anæsthesia, the site thoroughly curetted, and healing was prompt, with amelioration of all the symptoms.

The specimen was hardened in a 5 per cent. solution of formalin and sections prepared for microscopic study by Dr. E. A. Shumway. Considering the clinical history just referred to, the condition at the time of examination, and the fact that in the tumor were found small, round mononuclear cells, some pigment, and an alveolar arrangement, together with a tendency of the thickened surface epithelium to proliferate inward, it was thought that we were probably dealing with an alveolar sarcoma, which had developed from a pigmented nævus of the conjunctiva.

In May, 1903, nearly eight months after the operation had been performed, the patient was again seen, and examination showed a marked recurrence on the former site, which, according to the patient's statement, had first been observed two months before, or nearly six months after removal. The appearance of the recurrent growth was not red and angry-looking, as was the original, but of a much paler hue—in fact, markedly resembling a lump of paraffin covered by the delicately tinted conjunctiva.

Expectant treatment was employed, and a few weeks later somewhat similar but smaller patches appeared at the nasal and temporal margins of the left eye, together with three isolated enlarged papillæ of the conjunctiva of the upper lid, the latter now presenting a bluish-white appearance, as if covered by a thin layer of well-diluted milk.

Further study of the microscopic specimens of the original growth at this time, considering the clinical history in its later aspects, proved, beyond doubt, that the condition was spring conjunctivitis and not sarcoma. The subsequent history of the case has confirmed this opinion.

Dr. Shumway's report of the histological conditions is as follows:

The sections of the tissue measure 5 mm. by 2.5 mm. The greater portion of the growth is composed of a loose-meshed, fibrous connective tissue, which contains a moderate number of bloodvessels. It is covered by a thick layer of epithelial cells, which have a tendency to send inward processes of cells beneath the surface. Directly below the epithelial layer the mass is densely infiltrated with mononuclear round cells, and the bloodvessels contain a few polymorphonuclear cells. In places there are, in addition, larger, flat cells, which are arranged in nests and have the appearance of proliferated endothelial cells, such as are found in beginning alveolar sarcoma of the conjunctiva. Scattered between them is a small amount of light-yellow pigment. The majority of the cells, however, are small and represent ordinary lymphocytes, whose presence is due to irritation of the tissue. Some of them are broken down, their nuclei are

fragmented, and the neighboring connective-tissue bundles have an œdematous appearance. The mass is evidently a new-growth, simulating a fibroma, with a decided inflammatory infiltration. The presence of the proliferated endothelial cells and the pigment is suggestive of commencing alveolar sarcoma. Similar cells, however, were described in a case of vernal conjunctivitis reported by de Schweinitz and myself, published in the *University Medical Bulletin*, and, in view of the clinical appearance and history, this portion of the growth should be considered of minor importance, and the diagnosis made of growth at the corneal limbus due to spring catarrh.

The chief points of interest in the case are:

1. The clinical and microscopic appearances of the growth so greatly resembling sarcoma.

2. The confinement of the ocular variety of spring conjunctivitis to one eye for nearly three years before it made its appearance in the other.

3. The fact that spring conjunctivitis was present in one eye for two years and eight months before the symptoms became sufficiently characteristic to permit a positive diagnosis to be made.

4. That the clinical history must always be given consideration in the establishment of a diagnosis from the study of a microscopic specimen.

INVESTIGATIONS OF THE NEWER METHODS FOR DIAGNOSING UNILATERAL KIDNEY LESIONS.

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AND

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Cystoscopy at last seems to have gained its well-earned place among the reliable and scientific diagnostic methods. Even strong opponents to its use, as James Israel, are now converted into ardent advocates of its diagnostic value, but the same is not yet true of ureteral catheterization. It seems as if the opposition is generally headed by those unfamiliar with its technique; to them ureteral catheterization appears to be a procedure of unsurpassable difficulty. They admit the desirability of obtaining urine from either kidney separately, but claim this end may be obtained with less danger and inconvenience to the patient and with the same accuracy for examining purposes by one of the many clever devices known as urinary segregators. Whoever has worked with these instruments will admit that they are more bulky and their introduction therefore more painful and dangerous to the patient than any of the ureteral

cystoscopes in use. I. Cohn,[1] who conducted at Posner's clinic a number of experiments with nearly all urinary segregators brought to the knowledge of the profession, found that in some instances the instruments had to be withdrawn from the bladder on account of their causing severe pain to the patient while *in situ*. Whenever methylene blue or milk under low pressure was injected through one side of the separator, the fluid coming from the other side was soon afterward noticeably colored. Admitted that injection of a fluid under the lowest possible pressure may enter one of the bladder chambers, separated from the other merely by a very thin rubber wall, under different conditions from those where the urine emerges drop by drop from the ureter, still, these experiments prove conclusively that an accurate separation of fluids by these devices cannot be accomplished.

Lichtenstern,[2] who principally experimented with the two segregators devised by French authors (Luys and Cathelin), concluded that the thin and easily movable rubber membrane cannot always produce an accurate separation of the bladder in two parts.

Kummell[3] reports a case of a woman, where nephrectomy had been performed on the right side, in which, by the use of Luys' segregator, urine was obtained only from the right side. He concludes from the fact that, as very often, on cystoscopy, the ureteral openings are seen to be very close to each other or in abnormal location, results from the use of segregators must be inaccurate. His strongest argument against the promiscuous use of these instruments is that the urine is obtained indirectly and is mixed with material that may be in the bladder.

Our experience with the different segregators coincides with these statements. Urinary segregators should be restricted to the very few cases in which cystoscopy is impossible (bladders of children or those that cannot be cleansed for cystoscopical purposes). In ureteral catheterization we have a method easy of execution in most cases and not very painful to the patient if dexterously performed, while the results obtained are absolutely reliable. The term "dexterously performed" does not imply a more than ordinary skill. Here, as elsewhere, it is true that practice makes perfect. On the other hand, it may be stated that, once familiar with the method, one becomes an enthusiastic adherer to it, on account of the accurate, faultless, and quick diagnostic results obtained. In our experience, as in that of many others, ureteral catheterization can be successfully done in almost every case, provided that the examinations are carried out with the necessary patience and perseverance. One of our cases (Case X.) required many painstaking and tedious sittings before we succeeded in clearing the diagnosis, which only could have been accomplished by ureteral catheterization. We will show later that examinations with one of the segregators would have led to unreliable and faulty conclusions.

The cystoscopes for catheterization of the ureters, in use by the majority of workers in this field, are those designed by Albarran, Casper, and Nitze, all three being modelled after the same design, the idea of which belongs to Casper. In Nitze's and Albarran's instruments the movements of the ureteral catheter in the bladder can be directed at different angles by a knee mechanism attached to the distal end, which is controlled by a screw at the ocular end of the cystoscope. The French instrument unites in itself three different cystoscopical types, viz., the ordinary examining, the irrigating, and the catheterizing. The vesical end of the ureteral catheter can be easily moved into an angle of 180 degrees; the only disadvantages are its small field of vision and low illuminating intensity.

Nitze's cystoscope combines the cystoscopical types of irrigation and ureteral catheterization; but it has two advantages over Albarran's instrument, viz., its larger field of vision and its excellent light.

In Casper's ureteral cystoscope the movements of the vesical end of the catheter to different angles are accomplished by the fact that the catheter lies in a canal the upper wall of which is formed by a movable cover. The farther this cover is pushed toward the bladder, the narrower becomes the slit from which the catheter emerges and the greater becomes its curvature, and *vice versa*. This instrument has one great advantage over the two cystoscopes previously mentioned, viz., after having catheterized one ureter, a second catheter can be introduced through the instrument while it is *in situ*, with which the other ureter can be catheterized. The removal of the instrument after catheterizing is more easily accomplished than in the other instruments, as the tension on the catheter is avoided by the removal of the cover. Lately Casper has constructed a double-barrelled cystoscope for catheterizing both ureters.

Bierhoff[4] has devised a cystoscope carrying two catheters, which are under separate control. This instrument is of small calibre (23 F.), but only a catheter of a small diameter can be used. It also having two cannulæ, a double-current irrigation can be employed for changing the fluid in the bladder while the instrument is *in situ*.

Kelly's cystoscope is not described here, as its use is limited to females. To our knowledge, one more catheterizing cystoscope is in use in this country, that devised by Bransford-Lewis. We regret to say that our attempts at cystoscopy with this instrument have been unsatisfactory.

Our own work was mostly done with Nitze's cystoscope, preferably on account of its illuminating properties.

We do not wish to dwell here on the technique of ureteral catheterization, but desire to point out a few facts that proved to be valuable in our work. The bladder was, in some instances, so sensitive and its capacity so small that the first attempts at cystoscopy failed entirely. Whenever, after innumerable washings, the fluid seemed

to return from the bladder fairly clear, it had become very cloudy by the time the cystoscope was introduced. In Case X., where this difficulty was experienced, the bladder could not be filled with more than 60 c.c. to 90 c.c. of fluid under local anæsthesia. We succeeded, though, under spinal anæsthesia with 0.05 tropacocaine, in filling the bladder with about 150 c.c. of fluid, which remained fairly clear for a few minutes, so that the regions of the ureteral openings could be inspected. Only the left opening was recognized as such, and fluid was seen to escape from it. The other ureter was apparently buried in a patch of ulcerated tissue. After repeated examinations we learned to locate the presumable site of the ureter by taking our bearings from the left ureter and describing with the cystoscope an angle of 45 degrees along the sphincter, where, under normal conditions, the ureteral opening should be located. To this point the vesical end of the catheter was pressed under a rather sharp angle and thus introduced into the ureter. Four or five times in this manner the right ureter was catheterized, but never could the catheter be pushed farther than about four or five inches above the vesical opening. The catheter was repeatedly left a whole hour *in situ* without obtaining a drop of any liquid. Even aspiration with a large hand-syringe did not produce anything. Meanwhile, the left ureter had been successfully catheterized and the urine obtained from it subjected to the usual tests. Through a catheter passed to the bladder, while the ureteral catheter was in the left side, a few drops of pus and blood were obtained, too small a quantity for examining purposes. Finally, after many futile attempts, the catheter was passed to the pelvis of the right kidney, and, after waiting some time for fluid to appear, we aspirated again with a hand-syringe, which was readily filled with several drachms of pure pus.

If we in this case would have relied upon segregation, which, on account of the great irritability of the patient's bladder, probably never could have been accomplished, we certainly would have concluded that blood or pus appearing on the right side was due to the tubercular foci seen in the bladder. This case shows conclusively that a correct diagnosis was only possible by ureteral catheterization, which, if possible here, can be carried out in the vast majority of cases.

It is very important, after the catheter has entered the ureter, to push it forward under the control of the eye; it may otherwise be caught in its progress and fold up in the bladder unnoticed by the operator. This may be overcome by drawing back the catheter and giving its ureteral end another angle by means of the extravesical screw.

In the majority of cases the bladder was anæsthetized by 30 c.c. of a 4 per cent. cocaine solution, but in many instances no local anæsthetic was used, save a few cubic centimetres of the cocaine

solution in the posterior urethra. The passing of the catheter in the ureter was always found to be absolutely painless.

Much has been said against ureteral catheterization, on account of the danger of infection to healthy kidneys. If such a danger exists it must certainly be a very remote one or only occur very rarely. Margulies,[5] who reports on 200 ureteral catheterizations, has never seen any bad results, and particularly states that never after ureteral catheterization was a rise of temperature observed in patients whose temperature was normal before the examination. The same has been experienced by Casper, Albarran, and others. In our material once a chill followed by some increase of temperature was observed in Case IX., most decidedly caused by the more than usually severe instrumentation, for, in order to catheterize both ureters with Nitze's instrument, it had to be withdrawn and introduced again into the bladder with one catheter *in situ*.

For the verification of certain doubtful points in the diagnosis of renal functional capacity, we examined the blood and urines obtained by ureteral catheterization of a number of patients with presumably healthy kidneys.

The value of cryoscopy of blood, as well as of urine, for determining the function of the kidneys appears to be a mooted question, from the mere fact that the firm molecules in urine continually change in number with the varying blood pressure. The cryoscopical point of the urine of a patient examined soon after drinking large quantities of water will, of necessity, differ from that determined in the same patient under usual dietary conditions. This fact was demonstrated to us in Case IX., where an examination was made after the patient had taken a large amount of mineral water. Here were found low cryoscopical urine points, —0.63 and —0.83 against —1.1 and —1.2, when liquids only had been taken in quantities to which the patient had ordinarily been accustomed. We deduced from this the important fact that one cryoscopical determination is of little value, and that by repeated tests only, done under various physical conditions of the patient, can a somewhat safe conclusion be arrived at.

Little has been published in this country upon cryoscopy, but the few publications at hand unanimously state that this method permits of reasonable accuracy in diagnosing renal insufficiency and the type of renal lesion present,[6] and that one may solely rely upon cryoscopy to determine the condition of the kidneys, provided it is possible to obtain specimens by catheterizing both ureters.[7] These statements must be considered, from our experience, as being too radical. The real value, in our opinion, lies in the comparison of the points of either side.

From our limited material we learned that wherever, in unilateral kidney lesions, the cryoscopical urine-point was very low as compared with that of the presumably healthy side, it could be concluded

that one kidney was diseased. A striking illustration of this fact is given in Case VIII., where the right kidney gave —0.4, while the left side showed —1.2, which certainly could be only interpreted as an impaired function of the side with the low cryoscopical point.

Less conclusive are our results with the determination of cryoscopy of blood. Casper and Kummell, who have the widest experience on this point, state that molecular concentration of blood only varies where a bilateral renal affection is present. In unilateral kidney diseases, where one healthy kidney does the work of both, the blood-point was found in almost all cases to be a stable one, between —0 56 and —0.58. We have only obtained blood for our investigations in a small number of patients, and our results do not coincide with those of the authorities just mentioned. We are satisfied, though, that this is due to the inaccuracy of Beckmann's cryoscope, and possibly also to certain faults in our methods.

The phloridzin test was found to be equally as valuable in regard to comparative results in our few pathological cases. The statements of one of us upon the value of this test made in a previous paper[8] were found to be verified by subsequent larger experience with the method. Phloridzin is perfectly harmless. The separation of sugar from phloridzin takes place in the epithelial structure of the glomeruli and tubules of the renal cortex and nowhere else in the human organism. Watson and Baily,[9] in their report upon experiments with phloridzin on patients with normal and diseased kidneys, conclude that the phloridzin test gives accurate indications of the condition of renal function and of the existence of renal disease; but they also found the reverse to be true in a series of observations.

Our experience with the phloridzin test is that no absolute conclusion can be drawn from it upon the function of the kidneys, but that the value of the test lies in comparing results on both sides from urines obtained by ureteral catheterization. We are certain that the quantity of sugar excretion does not afford a safe guide as to the condition of the kidney. Neither are we prepared to claim any particular pathognostic value for the retarded appearance of sugar after the injection of the usual dose of phloridzin.

Israel, of Berlin, reports observations in which, after phloridzin injection, no sugar appeared in the urine. Barth,[10] in his report, mentions a case in which, without any plausible reason, no phloridzin reaction occurred where in a former examination the same dose of phloridzin had given a prompt positive result. We are, from our experience, inclined to think that the solution used in these instances was not fresh. Wherever we used fresh solutions of phloridzin we found sugar present in the urines one-half hour after the injection. In those cases where we got negative results, we injected the next day the same quantity of a new solution, and our results were positive for sugar.

As for urine cryoscopy, Case VIII. is also for the phloridzin test a striking example of its comparative value. Here we found on the diseased side 0.25 per cent. sugar, while the healthy side showed 1.28 per cent. This is such a striking difference that, other tests being equally conclusive, positive conclusions could be drawn from it.

Equally important seems to be the comparative study of quantitative values of urea excretion in urines separately obtained by ureteral catheterization. Unfortunately, our pathological material was too small to afford us sufficient proof for the verification of results obtained by others. (Kummell, Barth.) In our cases with normal kidneys the quantitative value of urea appeared to be almost equal.

Our microscopic findings of both urines were not without an element of grave error, caused by the fact that we only catheterized one ureter in almost all our cases, taking the bladder urine as representing the secretion of the other kidney for microscopic examination. This resulted in showing, in a majority of the cases, red blood cells, certainly caused by a mechanical lesion of the bladder wall, through the introduction of the cystoscope.

For the following reports the urine was obtained by catheterizing one ureter, removing the cystoscope, and passing a soft-rubber catheter to the bladder, care being taken that the bladder was empty before collecting specimens. The urine passing through the bladder usually contains blood, as above stated. A few red cells from the catheterized side may be also present, due to the passage of the catheter, it being withdrawn a short distance in taking out the cystoscope. This method does not alter the cryoscopical, urea, or phloridzin findings, but does not give accurate microscopic results, for the urine passing through the bladder may, besides blood, contain elements from that organ (pus, epithelial cells, etc.).

The cryoscopical examinations were made with a Beckmann's cryoscope, the thermometer being corrected often by testing with distilled water. We adopted the plan of placing the inner tube directly in the freezing mixture until the mercury dropped below zero before placing in the air chamber; by this procedure the time of freezing is shortened about one-half. For the blood cryoscopy we obtained from the median basilic vein about 20 c.c., allowing the blood to flow directly into the small tube of the cryoscope and agitating with the mixture wire, then proceeding immediately as with the urine. Although the points obtained by this instrument cannot be considered absolutely reliable, still, we found them to be sufficiently accurate for comparison. The amount of urea was estimated by the Doremus ureometer, and the findings given in milligrams per cubic centimetre. Just before catheterizing 20 minims of a $\frac{1}{2}$ per cent. phloridzin solution was given hypodermically. The phloridzin must be thoroughly dissolved and only a fresh solution used, for in some of the cases no sugar was found after

injecting an old solution. It is also well to add an equal quantity of Na_2Co_3 to keep the phloridzin in solution.

We found, as did Baily and Watson, that the most sugar is excreted during the first half-hour, and most of our estimations were made with this urine. We used Lohnstein's new saccharometers and found them very accurate for comparison, being able to detect a difference of $\frac{1}{100}$ per cent. Three instruments were used, one for the urine of each kidney and the third for a control of distilled water, so that the results might be obtained under the same conditions.

CASE I.—*July 2d.* Blood cryoscopy, —0.61; left ureter catheterized. Cryoscopy: Left kidney, —1.6; sugar, 0.77. Cryoscopy: Right kidney, —1.5; sugar, 0.85 (one hour after injection of phloridzin).

21st. Right ureter catheterized. Cryoscopy: Right kidney, —1.5; urea, 0.016; sugar, 0.35. Cryoscopy: Left kidney, —1.62; urea, 0.018; sugar, 0.3 (two hours after injection of phloridzin). Microscopic: Right kidney, few red cells, leukocytes, calcium-oxalate crystals, conical epithelium, bacteria. Left kidney, numerous red cells.

CASE II.—*July 14th.* Blood cryoscopy, —0.58.

16th. Right ureter catheterized. Cryoscopy: Right kidney, —1.8; urea, 0.012. Cryoscopy: Left kidney, —1.57; urea, 0.013 (sugar not present one, two, and three hours after injection of phloridzin, which had been in solution about ten days. Next day fresh solution gave positive results). Microscopic: Right kidney, few red cells, numerous round and conical epithelial cells; hyaline casts. Left kidney, numerous red cells, flat epithelial cells.

23d. Cryoscopy: Right kidney, —1.42; urea, 0.011. Cryoscopy: Left kidney, —1.75; urea, 0.013; sugar, not present. Phloridzin solution, old. (Next day fresh solution showed sugar.) Microscopic: Right kidney, red cells, calcium-oxalate crystals, flat epithelium. Left kidney, few red cells, round and conical epithelium, granular cast, bacteria.

CASE IV.—*July 28th.* Left ureter catheterized. Cryoscopy: Right kidney, —1.54; urea, 0.012; sugar, 1.32. Cryoscopy: Left kidney, —1.49; urea, 0.011; sugar, 1.3. Microscopic: Right kidney, red cells; flat, conical, and round epithelium; bacteria. Left kidney, few red cells, round epithelium, leukocytes, bacteria.

August 5th. Blood cryoscopy, —0.46.

CASE V.—*August 26th.* Right ureter catheterized. Cryoscopy: Right kidney, —1.44; urea, 0.015; sugar, 1.4. Cryoscopy: Left kidney, —1.22; urea, 0.0145; sugar, 1.1. Microscopic: Right kidney, round and conical epithelial cells. Left kidney, flat, round and conical epithelial cells; red cells.

The above sugar percentages were determined with urine passed during the first half-hour after phloridzin injection. The urine passed during the second half-hour showed 0.3 per cent. of sugar.

CASE VI.—*March 7th.* Left ureter catheterized. Cryoscopy: Right kidney, —1.33; urea, 0.0095; sugar, 0.45. Cryoscopy: Left kidney, —1.38; urea, 0.01; sugar, 0.6. Microscopic: Right kidney, pus cells, red cells, uric-acid crystals. Left kidney, red cells, uric-acid crystals.

The following cases are of pathological note and are, therefore, reported at length:

CASE VII.—J. F., aged thirty-five years. Family history: father died of pneumonia, uncle on father's side of tuberculosis. Previous history: typhoid fever six years ago; gonorrhœa several times, last attack eight years ago; orchitis five years ago.

Present illness began one year ago with œdema of lower limbs and some ascites, which disappeared after three weeks' treatment. Urine at this time showed albumin, hyaline and granular casts, round cells, pus cells, and red cells. Has been dropsical off and on since.

May 28, 1903. First saw patient; temperature, 96° F.; pulse, feeble; nausea; vomiting; diarrhœa. *Examination.* Patient emaciated, having lost twenty-five pounds in last year; heart and lungs negative; kidneys not palpable, but some tenderness on deep pressure over the right. Urine showed 0.2 per cent. albumin; numerous pus cells and tubercle bacilli. Pigs injected with this sediment gave negative results. Cystoscopic examination showed on the bladder-wall numerous patches of ulcerations.

July 11th. Right ureter catheterized. Cryoscopy: Right kidney, —0.95; urea, 0.0045; sugar, 0.25. Cryoscopy: Left kidney, —1.4; urea, 0.004; sugar, 0.2. Microscopic: Right kidney, pus, few red cells, round and conical epithelium, no tubercle bacilli. Left kidney, red cells, few pus cells, no tubercle bacilli. Patient's condition at this time not permitting further examination he was sent to the country, where he died three months later of uræmia. No autopsy.

CASE VIII.—A. H., aged fifty-five years; brewer. Family history negative. Has been a heavy beer-drinker. Previous history unimportant. Present illness began one year ago, when he passed bloody urine; this again occurred one month later. Six months ago, December, 1902, was confined to bed for three months, during which time the urine contained a large amount of blood; bladder became irritable, patient urinating every hour. Pain at the end of the penis. Chills, fever, and sweats at this time.

June 1st. Again passing blood; no pain; feels weak; constipation, alternating with diarrhœa. Has lost forty-five pounds. *Examination.* Poorly nourished; skin pigmented on right side of face and left thigh. Heart and lungs negative. Tumor palpable on the right side of the abdomen, about the size of an orange, smooth and slightly movable. No pain or tenderness on palpation.

July 10th. Right ureter catheterized. Cryoscopy: Right kidney, —0.4; sugar, 0.25. Cryoscopy: Left kidney, —1.2; sugar, 1.28.

Microscopic: Right kidney, numerous red cells and round epithelia. Left kidney, red cells, pus cells, and round epithelia.

16*th*. Right ureter catheterized; cryoscopy, —0.3.

18*th*. Left ureter catheterized; cryoscopy, —1.5.

21*st*. Blood cryoscopy, —0.55.

22*d*. Right kidney removed by Dr. Weil; about twice the normal size, irregularly contracted. Examination proved it to be a Grawitz tumor.

23*d*. Passed 560 c.c. of urine in first twenty-four hours.

24*th*. 800 c.c.; cryoscopy, —1.63.

This man made a good recovery, but his urine two months after operation still contained some red cells, which were thought by Dr. Jellinek, his attending physician, to be from the remaining right ureter. Further cystoscopic examinations were not permitted.

CASE IX. (By courtesy of Dr. L. Gross).—M., Japanese merchant; father has pulmonary tuberculosis. Previous history: malaria ten years ago; typhoid fever two years ago. Three months ago patient first passed blood, mixed with urine; no clots. This continued for a month intermittently, bloody for a few days, then clear. Urine remained clear if patient stayed in bed. Has had no pain, chills, or fever; appetite good, and general health not impaired. Passed urine about ten times during the day and twice at night. No blood within the last two months (since first catheterization of the left ureter, September 1st). Before examination patient passed about ten ounces of very bloody urine. After catheterization a great amount of urine was passed, the patient having taken a large amount of liquid during the day; this fact is mentioned in order to account for the low cryoscopic points.

Left ureter catheterized. Cryoscopy: Right kidney, —0.62; urea, 0.007; sugar, 1.05. Cryoscopy: Left kidney, —0.83; urea, 0.01; sugar, 1.5. Microscopic: Right kidney, pus cells, few red cells, flat and round epithelial cells. Left kidney: numerous red cells, round epithelia, and casts.

September 14*th*. Blood cryoscopy, —0.51.

Sept. 23*d*. Both ureters catheterized. Cryoscopy: Right kidney, —1.1; urea, 0.0075; sugar, 0.6. Cryoscopy: Left kidney, —1.2; urea, 0.0095; sugar, 0.5. Microscopic: Right kidney, few red cells, crystals of uric acid; sediment, small amount. Left kidney, numerous red cells.

Both examinations did not prove satisfactorily the presence of any pathological condition. Whether the hæmaturia was due to a kidney or ureteral condition we cannot say, but the findings of the second examination show conclusively that the renal function was not at fault. Operative procedure was advised against, and at the present time, two months and a half after examination, the patient has had no return of his hæmaturia and is in excellent health.

CASE X. (By courtesy of Dr. Jellinek).—J. M., aged thirty-nine

years; farmer. Mother and one brother died of pulmonary tuberculosis. Nineteen years ago took care of tubercular brother, after which he became ill and was told he had pulmonary tuberculosis; since then until the present trouble has lived an out-of-door life and has been in good health. One year ago noticed some trouble on urination; passed blood two or three times in one day. Health became impaired, but had no urinary symptoms, with the exception of a little pain in the region of the bladder, until four months ago. Then had pain on urinating, which occurred about every hour, day and night. Urine became very foul-smelling. Condition on admission to the German Hospital, about two months ago: poorly nourished, nervous, unable to sleep, night-sweats, irregular temperature, continuous pain in bladder region, more marked at the end of urination. Heart negative; tubercular involvement of apex of right lung; appetite fair; no trouble with digestion; passes urine about every hour, which contains abundance of pus and tubercle bacilli. Pigs injected with this sediment died of tuberculosis.

September 25*th*. Cystoscopy: numerous ulcerated patches over bladder-wall; left ureter catheterized; a good quantity of urine obtained, but nothing came from the bladder catheter that could be utilized. Cryoscopy: Left kidney, —0.9; sugar, 0.4. Microscopic: Some pus, round epithelia, few uric-acid crystals, bacteria, no tubercle bacilli.

October 24*th*. Right ureter catheterized, and over an ounce of greenish-yellow pus obtained, which contained tubercle bacilli.

26*th*. Urine cryoscopy: bladder urine, —1.08.

November 4*th*. Operation (by Dr. Weil). Right kidney about twice normal size, lower portion fluctuating; about eight ounces of greenish-yellow pus removed; kidney drained.

8*th*. Passed thirty-eight ounces of urine in last twenty-four hours; large amount of pus; cryoscopy, —1.12.

Case XI.—S. S.; previous history unimportant.

March 18*th*. Attack of severe pain on left side, which necessitated giving morphine ($\frac{3}{4}$ grain) for relief; complete anuria for twenty-four hours. From the symptoms a diagnosis of renal calculus was made. The first urine passed showed a trace of albumin, numerous red cells, leukocytes, and uric-acid crystals. Condition gradually improved, so that on March 25th normal amount of urine was passed.

August 18*th*. Another attack of pain, but less severe; slight chill, urine diminished to twelve ounces, contained trace of albumin, amorphous urates. After four or five days the patient was able to get about again, and has remained in good health since.

30*th*. Left ureter catheterized. Met with resistance about five inches from the bladder, beyond which point the catheter could not be passed. Cryoscopy: Right kidney, —1.31; urea, 0.0085; sugar, 2.8. Cryoscopy: Left kidney, —1.47; urea, 0.008; sugar, 2.8.

Microscopic: Right kidney, flat epithelium, uric-acid crystals, red cells. Left kidney, round epithelium, uric-acid crystals, numerous red cells.

We have presented this rather small material because we believe that in the diagnosis of unilateral kidney lesions any contribution is of value. As we have stated above, none of the methods for determining the functional capacity of the kidneys enable us to arrive at a conclusion upon the actual function of both kidneys or either organ. In other words, none of these methods alone are sufficiently accurate to decide upon the basis of one of them the question whether a kidney should be removed or not. The real value of the methods worked out in our material lies in the comparative results and in the coincidence of the methods. A "conditio sine qua non" for the application of these methods is ureteral catheterization, and wherever feasible, catheterization of both ureters. If both urines obtained in this way are subjected to cryoscopy, phloridzin test, urea examination, and microscopic examinations, we are certainly enabled to get a fair idea upon the functional value of either kidney and to arrive at safe conclusions from our findings as to intended operative procedures.

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THE PRODUCTS OF GLYCOLYSIS IN BLOOD AND OTHER ANIMAL FLUIDS.

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IT is a well-known fact that normal blood of almost all species of animals when freed fresh from its albumins shows a reducing body which is unquestionably largely made up of dextrose. When, however, the blood is allowed to stand some time, even when kept free from bacterial decomposition by antiseptics (thymol), this reducing

body disappears, and only a substance which is able to hold copper in solution in an alkaline medium is found, but no reduction takes place. Biernocki, Pavy, and Lepine have shown further that if dextrose be added to blood under similar conditions, not only is the blood-sugar destroyed, but also a large proportion of that which has been added. To this process they give the name of glycolysis. My attention had been directed to the fact, and efforts had already been made by me to determine what became of the sugar thus destroyed, when, in 1901, P. Mayer[1] demonstrated that ox blood contained paired glycuronic acid, one of the oxidative products of dextrose, and very closely allied to it, and Mayer[2] further showed that if glycuronic acid be given to an animal and oxidation be experimentally restricted, saccharic acid is eliminated. It has also been demonstrated by the same author that if glycuronic acid or even dextrose be given in great excess, an increase of oxalic acid is found in the urine, and also that the liver is found to be surcharged with the same acid, from which he deduces the principle that if there is present an actual or relatively diminished oxidation (overwhelming the organism with carbohydrate) these partially oxidized products will appear in the urine. Based upon these facts, my efforts were directed toward determining whether the products of the so-called glycolysis of the blood might be any of these substances, viz., glycuronic, saccharic, oxalic, or carbonic acid, the final product of oxidation; of these the three last do not reduce Fehling's solution, which would account for the loss of the blood sugar in blood which is allowed to stand.

Experiment 1.—570 c.c. hydrocele fluid which had been kept two weeks on ice, was precipitated by twice its volume of 95 per cent. alcohol, filtered and washed, the alcohol driven off, acidified with acetic acid, boiled, and filtered. The resulting fluid did not show any immediate reduction with Fehling's solution, such as would be expected of dextrose. For the purpose of isolating the supposed carbohydrate body, the method of Salkowski, for obtaining xylon[3] was used, but the resulting product was a blue syrupy fluid which could not be made to crystallize, but which, when again dissolved in sodium hydrate, reduced promptly upon warming. The peculiarities of this substance suggested that it was glycuronic acid, but it was not proven. The copper suboxide formed (0.148 grams) showed 0.0667 gram of reducing body reckoned as dextrose.

Experiment 2.—500 c.c. fresh ox blood was precipitated by alcohol as before, and an effort made to isolate the reducing body by the same means as before, but ineffectually, since no precipitate could be obtained.

Experiment 3.—(*a*) 100 c.c. fresh ox blood as control for the following was precipitated with alcohol, the resulting filtrate freed

[1] Zeit. f. phys. Chemie, vol. xxxi.
[2] Berlin. klin. Wochenschr., 1899, pp. 27, 28.
[3] Zeit. f. phys. Chemie, vol. xxxiv. p. 162.

from alcohol and warmed with 40 c.c. Fehling's solution. There was no immediate precipitate, but twenty-four hours afterward a whitish-yellow precipitate had formed, but it was too small in amount to furnish identification.

(*b*) 500 c.c. of the same ox blood as above was charged with 5 grams of dextrose and allowed to remain in the same brood-oven at a temperature of 38° C. for forty-five hours, decomposition being avoided by the addition of toluol. By that time it had acquired a deep purple color, and after the toluol had been driven off over the water-bath, it was freed from albumin by alcohol, the precipitate again rubbed up with alcohol in a mortar, the alcoholic extracts united, and the alcohol removed by distillation. After establishing the volume at 1000 c.c., 50 c.c. of this clear fluid was cooked with Fehling's solution, but no reduction took place, nor was there any reaction with phloroglucin or orcin. This liquid was then allowed to stand several weeks in the refrigerator, whereupon it was filtered from the slight precipitate formed, reduced to 500 c.c. by evaporation, and then treated with subacetate of lead and ammonia; the precipitate removed, washed, suspended in water, acidified with acetic acid, and the lead removed by sulphuretted hydrogen, and the fluid reduced to 50 c.c. at 40° C. This had no reducing power, did not modify the light in the polariscope, and the remaining 40 c.c. when distilled with an equal amount of hydrochloric acid gave no furfurol with phloroglucin in the distillate; from this it is safe to say that while the dextrose was wholly converted it must have passed beyond the stage of glycuronic acid, either into a volatile substance like CO_2, or into the less readily identified carbohydrate acids.

Experiment 4.—(*a*) In order to determine whether the blood-sugar or added dextrose was converted into carbon dioxide, the final product of oxidation, as well as of yeast fermentation, 1 litre of fresh ox blood to which toluol has been added, and in a stoppered flask from which a tube led into a flask containing barium hydrate solution, which was protected from the outer air by a drying tube containing sodium hydrate, was allowed to remain in the brood-oven for twenty-four hours. When removed some insoluble barium carbonate had been formed in the adjoining flask, which was tightly stoppered and placed on ice until opportunity offered for the determination of the carbon dioxide. The blood was freed from albumin by the method of Abeles (zinc acetate and absolute alcohol), the zinc removed and the solution concentrated to 250 c.c. at 40° C. The solution had a left-turning power of 0.05 per cent. reckoned as dextrose, and gave a faint phloroglucin and orcin reaction, but no lines in the spectroscope, even when shaken out with amyl alcohol. It was now precipitated with lead and ammonia, and, after removal of the lead, concentrated to 50 c.c. Its turning power was now lost; it gave still a weak orcin and phloroglucin reaction, but no spectroscopic lines, and an osazone which was largely soluble in absolute

alcohol. The barium carbonate which was formed in the barium hydrate solution was removed and the carbon dioxide determined according to Fresenius (*Quantitative Analysis*, vol. i. page 439). It amounted to 0.1054 gram in the litre of blood.

(*b*) 5 grams dextrose were added to 1 litre of the same blood as above and under the same conditions, the mixture was allowed to remain in the brood-oven the same length of time. It was then removed and treated in the same way. The resulting fluid, which was free from albumin, gave a weak phloroglucin and orcin reaction, did not reduce, but kept copper in solution in alkaline medium, and had no turning power. It was then treated as before, with lead and ammonia, and the resulting fluid concentrated to 50 c.c. It now gave a much stronger Tollens reaction, but no spectroscopic lines, and still had no turning power. The amount of carbon dioxide, determined in the same way, which had been given off was 0.1163 gram. In this case we see that 5 grams dextrose had utterly disappeared, and yet it could not have been converted into carbon dioxide, for the amount of this in the latter instance was but a trifle more than in the former, or 0.1163 gram as compared with 0.1054 gram, and in both cases it may have come from the blood itself, since Ludwig, Pfleuger, and others have found as much as 40 per cent. in dog's arterial blood.

Experiment 5.—(*a*) 5 grams dextrose were added to 250 c.c. fresh hydrocele fluid—obtained through the courtesy of Dr. Gardner W. Allen—connected with a carbon-dioxide apparatus, and the whole placed in the brood-oven for eighteen hours. It was then removed, and, without disconnecting from the apparatus, air was drawn through the blood for thirty minutes. It was then poured into an equal amount of a solution, saturated when warm with both sodium chloride and mercuric chloride, allowed to stand overnight, filtered, washed, and the filtrate and wash water freed from mercury reduced to 250 c.c. It now gave a marked phloroglucin reaction, with a line in green in the spectroscope, had a right-turning power equal to 0.5 per cent. as dextrose, and a reducing power which was equivalent to 0.66 per cent. dextrose, determined according to Allihin. Its carbon dioxide equalled 0.0804 gram.

(*b*) 10 c.c. of the same fluid taken as control and immediately precipitated, had a slight reducing power, gave no Tollens reaction, had a slight dextrorotatory power, and gave a fine, yellow, needle-like osazone, which was mostly soluble in absolute alcohol. As can readily be seen, 3.35 grams of the dextrose added to this fluid disappeared, forming no carbon dioxide, for this amount of sugar by fermentation would produce, theoretically (43.3 per cent.), 1.45 grams carbon dioxide, instead of the 0.0804 gram found, but glycuronic acid presumably, since, when paired, being a left-turner, it reduced the actual amount of carbohydrate 0.66 per cent. to 0.5 per cent. in the polariscope and gives a marked Tollens reaction.

EXPERIMENT 6.—(*a*) 1 litre fresh beef blood was placed in a flask connected with a carbon-dioxide apparatus, toluol added, and the whole placed in the brood-oven for twenty-two hours, air drawn through for thirty minutes, and then freed from albumin by sodium and mercuric chloride, and the latter removed. The resulting clear fluid was then reduced to 50 c.c., which had no turning power, but a reducing power equal to 0.0586 gram of dextrose, or 11 per cent. The remainder was then cooked in an autoclave with 1 per cent. sulphuric acid for one hour and neutralized, whereupon it acquired a dextrorotatory power of less than 0.1 per cent. It formed an osazone of lemon-colored needle-like crystals mixed with globules of a darker hue, which were almost entirely soluble in absolute alcohol. The original blood emitted 0.1878 gram carbon dioxide.

(*b*) To another litre of the same blood 5 grams dextrose were added in a flask which was connected with the carbon-dioxide apparatus, and the whole placed in the brood-oven as before for the same time. It was then freed from albumin and reduced to 50 c.c. It was levogyr to 0.1 per cent., and had a reducing power equivalent to 0.0591 gram, or 0.118 per cent. as dextrose. The remainder was now cooked with sulphuric acid, but it remained a left-turner and gave a marked phloroglucin and orcin reaction without spectroscopic lines. It gave an osazone consisting of a few crystals (needles), but chiefly of globules, which were soluble in absolute alcohol. Its carbon dioxide amounted to 0.9564 gram.

(*c*) 1 litre of the same blood was precipitated at once and reduced to 50 c.c. It then had a turning power of +0.1 per cent. and a reducing power of 0.0403 gram as dextrose, or 0.08 per cent. It formed an osazone soluble in alcohol, consisting of irregular, feathery masses.

In both (*a*) and (*b*) the fact that the rotatory power was less than the reducing power and that (*a*) was converted to a dextrogyr body and that (*b*)'s levogyr power was very much lessened by splitting with sulphuric acid shows that at least a portion of the reducing substance was in the form of glycuronic acid, a fact still further emphasized by the marked orcin and phloroglucin reaction in (*b*), which, based upon its reducing power and compared with the control (*c*), had lost all of the dextrose added. A part of this may have been converted to carbon dioxide, since there was a marked increase in this over (*a*), to which no dextrose was added. As is well known, the paired glycuronic acid being a left-turner, diminishes or obliterates the dextrogyr power of dextrose.

EXPERIMENT 7.—(*a*) 1 litre of a pleuritic exudate, obtained through the courtesy of Dr. Mackechnie, guarded against decomposition by toluol, was placed in the brood-oven for twenty hours, removed, freed from albumin by the mercury process, and reduced to 200 c.c. The rotatory power was now +0.1 per cent. and the reducing 0.23 per cent. as dextrose. There was no Tollens reaction.

The fluid was then cooked with sulphuric acid, after which it still retained a rotatory power of +0.1 per cent.; Tollens weak. In producing the osazone in this and all the following experiments a strict proportion between the phenylhydrazin added and the amount of reducing body, as determined by the polariscope after splitting, was maintained, so that one molecule of the reagent was added to one molecule of the suspected glycuronic acid, which, according to their molecular weights, gave 0.55 gram of the reagent to 1 gram of the substance sought, or as my reagent was in the form of the chloride, 0.735 gram was used. Another improvement which was suggested by Neuberg was to place the substance and reagent in a brood-oven for twelve to fourteen hours instead of boiling it, and this proved very satisfactory in increasing the product and avoiding tenacious masses, which would form on the edges of the flask in the old way. This limited addition of phenylhydrazin is supposed to cause the glycuronic acid to form an osazone to the exclusion of dextrose, or, if the latter does form, it can be separated by washing with hot water and absolute alcohol. It is true that Neuberg and Mayer use bromphenylhydrazin, but I think I have demonstrated that the ordinary reagent can be used in the same way.

(*b*) 10 grams of dextrose were added to 1 litre of the same exudate and the whole placed in the brood-oven for the same time as before, then freed from albumin and reduced to 200 c.c. Polariscope showed +0.7 per cent. and reduction 1.201 per cent., while there was no phloroglucin and no orcin reaction. After cooking with sulphuric acid, rotatory power 0.75 per cent. as dextrose, both orcin and phloroglucin positive, and osazone of well-formed globules of dark color.

(*c*) 400 c.c. same exudate freed at once from albumin and reduced to 50 c.c. Polariscope showed +0.2 per cent. and reduction 0.35 per cent. After splitting polariscope showed +0.25 per cent., but there was no Tollens reaction. Attention must be called here to these general features repeated in the other experiments; the reduction is greater than the polariscopic reading in (*a*) and (*b*); the Tollens reaction is brought out strongly by the splitting with sulphuric acid, as is also an increase in the polariscopic reading. It becomes evident, also, that during the process of evaporation, even if the reaction is kept slightly acid, as was the custom, a partial splitting of the paired acids takes place, else we should much oftener come across levogyr bodies. The separation of the glucosazone from the combination of glycuronic acid and other acids with phenylhydrazin could be accomplished with repeated washings with hot water and after drying with absolute alcohol upon the filter paper. The wash water and alcohol upon cooling would often cause a precipitation of a crystalline nature, which consisted almost entirely of glucosazone, and its needles are very different from the globules which the other compounds form. The demonstration of the nature

of the precipitate, which is insoluble in hot water and absolute alcohol, was most difficult. Since the glucosazon is soluble in absolute alcohol, presumably the residue which was left was an hydrazin of glycuronic or saccharic acid, but no solvent could be found which would enable one to determine its power in the polariscope. Mayer and Neuberg use a mixture of absolute alcohol and pyridine, and its left-turning power is so great (0.2 gram in 10 c.c. of the mixture gives a reading of —7° 25′) that it can be easily distinguished from all other osazones or hydrazins, but the pyridine could not be procured, and after various attempts to find a solvent in mixtures of glacial acetic acid, acetone and absolute alcohol, the attempt to identify the substance in this way was abandoned. It suffices to say, however, that the insoluble portion had all the characteristics of the hydrazin of glycuronic acid described by Mayer.[1]

Another fact worth mentioning is that the product obtained with phenylhydrazin from the normal blood was perfectly soluble in hot water and alcohol, while that from both bloods subjected to the brood-oven temperature was only partially so. In no case was there sufficient evidence that more than an infinitesimal amount of the lost dextrose was converted to the carbohydrate acids, and we must fall back upon the suggestion made that the dextrose may combine with the albumin of the blood and be removed with that.

The next point to establish was whether the dextrose could have been converted to oxalic acid by the process of glycolysis, as is assumed by Mayer, in the animal when oxidation is impaired. For this purpose four portions of fresh ox blood were taken and treated in the following manner:

(*a*) 1 litre was precipitated at once by mercuric and sodium chlorides, the mercury removed, and, keeping the steadily increasing acid reaction in check by sodium carbonate, the whole was reduced to 200 c.c. It was then shaken three times with ether, no hydrochloric acid having been added on account of that present from the mercuric chloride removed, and an effort made to determine the oxalic acid, if present, according to the method of Salkowski; but only the merest traces of this substance were found too small for estimation. The remaining watery solution was freed from ether and reduced to 50 c.c., when its turning power was found to be +0.2 per cent., while by the method of Allihin there was found to to be 0.199 per cent., or practically the same as shown by the polariscope. It gave no reaction with phloroglucin. It was then split with 1 per cent. sulphuric acid in a closed flask, and the volume having been re-established, with due calculation for the amount used in the reduction determination, it now gave a turning power of +0.15 per cent., and afforded, dried at 110° C., 0.0888 gram of an osazone which dissolved in 3.5 c.c. glacial acetic acid, gave a turning power of —0.2

[1] Zeit. f. Physiol. Chemie, 29, 67.

per cent. reckoned as dextrose. From all the evidence found here probably nothing but dextrose existed in the blood.

(*b*) 1 litre of blood, to which 10 grams of dextrose were added, was attached to a water-pump, after having been treated with toluol, in hopes of at least partially preventing decomposition, and air was drawn through it for twenty-four hours. It was then freed from albumin in the same way, reduced to 200 c.c., and shaken three times with ether, in order to extract the oxalic acid, but only traces were found. The ether was driven off from the watery solution, and the whole reduced to 50 c.c. Its turning power was now +1.875 per cent., and it gave the phloroglucin but not the orcin test. By the Allihin method with copper it showed 1.54 per cent. of a reducing body; a peculiarity in the reduction was noticed which is suggestive of glycuronic acid, as well as other substances apart from dextrose. The Fehling solution became at first greenish when boiled, and a yellowish precipitate was thrown down, in which were seen particles of the red suboxide of copper. Owing to the fact that on evaporation a large amount of salts had been thrown out of solution and the possibility that some dextrose was mechanically held by this mass from which it had been filtered, these were extracted with water until the last water showed no reduction. The volume had now risen to 225 c.c., giving a polariscopic reading of +0.51 per cent., which was cooked in a closed stone flask for eight hours with 1 per cent. sulphuric acid. This solution, when neutralized, possessed a turning power of +0.425 per cent. and both the phloroglucin and orcin reactions, but no lines. It also gave, dried at 110° C., 1.244 grams of an osazone or hydrazin, consisting of microscopic rosettes and globules, which was insoluble in hot water and absolute alcohol, whose optical properties could not be determined, as before stated, for want of a suitable solvent. In this, as in previous instances, an attempt was made to determine the nitrogen by Kjeldahl, but, though the destruction of the substance by the acid seemed complete, no ammonia could be distilled over; yet it is not safe to judge from this that no nitrogen existed in the compound.

(*c*) This litre of blood, treated with toluol, was allowed to remain at brood-oven temperature for twenty-four hours without the addition of dextrose, freed from albumin, reduced to 200 c.c., an almost neutral reaction having been maintained, shaken out with ether, freed from the same, concentrated to 50 c.c., and tested for reducing bodies. No oxalic acid was found beyond the mere traces mentioned in the other samples. It showed no reduction, no turning power and phloroglucin test, hence no further attempts were made to isolate an osazone. It simply proves what has been so often established, that a blood loses its native dextrose, even when by strong antiseptics the possibility of fermentation is practically excluded, without leaving any traces of discoverable oxidative or glycolytic products of the dextrose which has disappeared.

(*d*) 1 litre of blood, to which was added 10 grams of dextrose and sufficient toluol to cover surface of the fluid, was placed in a brood-oven for twenty-four hours and treated as before. No oxalic acid was found, but it gave a marked phloroglucin reaction. The polariscope showed, in 100 c.c. of fluid, 0.503 per cent., while by reduction of copper and weighing, 0.5 per cent. was found. The remainder after these tests was diluted again to 100 c.c., showing a turning power of +0.15 per cent., and after splitting with 1 per cent. sulphuric acid, +0.2 per cent. It also gave marked phloroglucin and orcin reactions, as also 0.370 gram of an hydrazin, insoluble in hot water and absolute alcohol. Here we have no decided increase of reduction over polariscopic reading, as would be present were the levogyr paired glycuronic acid present to any extent, nor do we find a marked increase of turning power after splitting with acid, as would be expected under the same conditions. We do, however, find an insoluble hydrazin and Tollens reaction, particularly after splitting, in both cases where dextrose has been added. Taken all in all, there is evidence that paired glycuronic acid exists in ox blood, as demonstrated by Mayer, and human serum, but none to substantiate the conversion of dextrose into that substance by means of any glycolytic ferment existing in the blood. We think that we have also demonstrated that the large amount of dextrose failing to reappear in these experiments is not converted into carbonic acid or oxalic acid. Where this change takes place, if it does, as insisted upon by Mayer, we do not know. One thing is evident to everyone who has worked with blood: that our means of separating the albumin are crude, and that the enormous coagulum or precipitate formed by the albumin must of necessity carry with it a considerable portion of the blood-sugar which cannot be separated from it. The problem of what becomes of the sugar in glycolysis still remains to be solved.

The methods of isolating the rarer forms of the oxidative products of dextrose, like glycuronic and saccharic acids, are still so crude that they offer but little hope of success in this direction. A glycolytic enzyme undoubtedly exists in the liver, but its action has been demonstrated on glycogen only, and can probably have nothing to do with the oxidation of dextrose. Croftan also claimed to have found an enzyme in the leukocytes which would destroy dextrose, but, beyond demonstrating that the sugar disappeared, nothing further was proved. Salkowski suggests that the oxidase which is found in the tissues may be the active agent, but, as far as I can learn, this agent has only been able to oxidize the more highly oxidizable bodies, like benzaldehyde and salicyldehyde, but never dextrose. The proof of the former action has been established by the detection of benzoic and salicylic acids; but, as far as can be learned, never of the latter by the detection of glycuronic, glycuric, saccharic acids, etc., the oxidative products of dextrose.

THE BACTERIAL EXAMINATION OF 104 SAMPLES OF WATER:

TOGETHER WITH A DETAILED STUDY OF THE COLON BACILLUS.[1]

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There does not appear to be a subject at the present time that is shrouded with a greater uncertainty than the sanitary interpretation of the presence of bacilli coli in a water supply. This uncertainty has been largely augmented by the fact that many reliable observers have found colon bacilli in waters which, presumably, were not polluted with fecal material.

At the meeting of the American Public Health Association at New Orleans, La., after considerable consultation between many of the laboratory workers, it was decided that several should conduct, independently, an investigation along the following lines:

1. The consideration of what should constitute a colon bacillus.
2. The amount of water most advisable to test in order to arrive at some conservative conclusion as indicating the presence or absence of fecal pollution.
3. The length of life of the colon bacillus in water under its natural environment.
4. The degree of frequency with which colon bacilli can be found in different amounts of water known to contain sewage.
5. To ascertain, if possible, the relative degree of frequency with which colon bacilli can be detected in water presumably not polluted with sewage.

After considering the subject, it appeared to the writer that his residential district was most fortunate, in that it afforded a favorable field for an investigation of this character, and, after obtaining the co-operation of an able laboratory assistant who could devote his entire time to the work, an investigation was started.

During the progress of the work many difficulties were experienced, and particularly was this true in considering the fifth division of the work, for the reason that, although many wells were found which, upon inspection, did not reveal the probable access of fecal pollution, it was impossible to locate but one body of water (Lake Hemlock, near Rochester) where sewage pollution could presumably be eliminated.

The first division of the work, as to what constitutes a colon bacillus, was conducted along the following lines:

[1] Read at Washington, D. C., October 26, 1903, before the Laboratory Section of the American Public Health Association.

1. An organism responding to the full colon test was isolated from fifteen different samples of human feces. These organisms were cultured in all the common media and in different lots of the same media, and the comparative results checked. It was found that the same organism in the same class of media, but of different generations (and particularly was this true in regard to the use of the Smith fermentation tube), would frequently differ as to the amount of gas produced during a definite interval. In two instances organisms giving indol and odor reactions in older generations would fail in different lots of the same class of media in earlier generations. It was the writer's endeavor by this procedure to ascertain as near as possible the actual degree of uniformity of results that it was possible to obtain with the present colon test.

2. In ascertaining what constitutes a colon bacillus was the study of certain lactic-acid producing organisms and their comparison with known colon bacilli. Many of the members of this section will recall that Prescott has pointed out a great similarity between certain lactic-acid organisms found upon grain and the colon organism.

The writer at the meeting of the American Public Health Association at New Orleans, La., exhibited cultures showing the similarity in the cultural manifestations between the bacillus acidi lactici of Hoeppe and the colon bacillus. The work in this connection was conducted as follows:

Fifteen different laboratories were communicated with and cultures purporting to be lactic-acid bacilli were received. After thorough cultural investigation it was impossible, by any of the usual methods, to demonstrate a constant difference between ten of the cultures received and the colon bacillus. These results at first puzzled the investigators, for it suggested the possibility of the lactic-acid organism not being a distinct species of the bacteria. It is now the writer's belief that such cultures were none other than colon bacilli mistaken for the lactic-acid organism, for the reason that the remaining five cultures contained an organism absolutely non-motile; nor was it possible, under different modes of procedure, to cause these organisms to develop motility, and they in that manner differed from the colon bacillus. It is the writer's opinion that such cultures were true lactic-acid bacilli, and this has been recently strengthened by the positive demonstration of spores in four of the five cultures.

3. The next step as to what should constitute a colon bacillus was devoted to the use of presumptive tests. This work was carried on to ascertain to what degree it was necessary to carry on confirmative work in order to arrive at a positive diagnosis where a presumptive test was most marked. The organisms tested were two common to most waters, namely, the bacillus fluorescens liquefaciens and the bacillus fluorescens putridus. All results were checked with cultures of colon bacilli.

The presumptive test included the use of three fermentation tubes containing 2 per cent. of dextrose bouillon and the subsequent testing of gas formulæ after forty-eight hours, the production of acidity, the coagulation of milk, the production of indol, and the production of a disagreeable odor. It was found that the organisms mentioned gave results that could be easily mistaken for colon bacilli, if no greater time than forty-eight hours be allowed and the exact morphology of the organisms not determined.

The result of this division's work seems to justify the following conclusions:

(*a*) That the factors liable to great variation in tests for colon bacilli are those pertaining to the amount of gas produced, the production of indol, and the production of a putrefactive odor.

(*b*) That it is necessary, in order to arrive at a positive diagnosis of colon in water, to completely culture the organism, and the results obtained include the following:

1. A motile organism.
2. Slender rods without spores.
3. An acid-producing organism.
4. One that will coagulate milk within forty-eight hours without a redigestion of the casein.
5. An organism producing marked turbidity in broth within twenty-four hours.
6. An organism capable of fermenting 2 per cent. of dextrose bouillon in a Smith fermenting tube giving 25 per cent. to 75 per cent. gas production within forty-eight hours, the gas having an approximate formulæ of two parts hydrogen to one part carbon dioxide.
7. The production of indol.
8. The reduction of nitrates to nitrites.
9. The production of a putrefactive odor.
10. An organism that will ferment lactose and saccharose as well as dextrose.

(*c*) That there are other organisms common to water which may be easily mistaken for colon bacilli if presumptive tests are alone considered.

The second division of the work, as to the amount of water advisable to test in order to indicate the presence or absence of fecal pollution, was conducted as follows:

Buffalo, a city of 400,000 inhabitants, is situated at the head of the Niagara River. This river has an average velocity of nine miles per hour, and, although a rapidly running stream, is not of excessively great volume. The sewage of Buffalo is emptied into this river, and, in consequence of its being a turbulent stream, becomes mixed with the water of the river in a very short distance. It appeared to the writer that examination of different amounts of the water at distances of twelve and twenty-two miles down the stream

would be productive of much valuable information as regards the amount of water advisable to test, as this river certainly received a tremendous amount of direct sewage pollution.

The investigation covered an examination of 104 samples. Fifty-two of these samples were collected twelve miles below Buffalo and the remaining fifty-two samples ten miles below this point, or twenty-two miles down stream. All samples were examined in quantities ranging from $\frac{1}{10}$ of a c.c. to 1 litre.

The results obtained were as follows: From the samples collected twelve miles down stream colon bacilli were present in:

21	per cent.	when	the	amount	examined	was . . . . 1/10 c.c.
29	"	"	"	"	"	. . . . ½ "
52	"	"	"	"	"	. . . . 1 "
59	"	"	"	"	"	. . . . 5 "
69	"	"	"	"	"	. . . . 10 "
80	"	"	"	"	"	. . . . 50 "
87	"	"	"	"	"	. . . . 100 "
90	"	"	"	"	"	. . . . 500 "
91	"	"	"	"	"	. . . . 1 litre.

Of the samples collected twenty-two miles down stream the results were as follows:

19	per cent.	when	the	amount	examined	was . . . . 1/10 c.c.
21	"	"	"	"	"	. . . . ½ "
34	"	"	"	"	"	. . . . 1 "
39	"	"	"	"	"	. . . . 5 "
41	"	"	"	"	"	. . . . 10 "
47	"	"	"	"	"	. . . . 50 "
51	"	"	"	"	"	. . . . 100 "
53	"	"	"	"	"	. . . . 500 "
59	"	"	"	"	"	. . . . 1 litre.

There were several doubtful results during the progress of the work, and all such results were recorded as being positive.

In several instances, if the presumptive test mentioned in Division No. 1 was alone considered as being conclusive evidence of the presence of colon bacilli, many errors would have resulted, and a much larger percentage of positive results recorded. As it is, the result of this work does not correspond with similar work conducted by Winslow and Miss Hunnewell, as recorded in a statement issued by Prescott, in that the percentage of 1 c.c. of samples examined revealing positive evidence of colon bacilli are much larger than in their investigation. This may be accounted for by the fact that it is the writer's belief that the relative frequency of colon bacilli in a given quantity of water is largely dependent upon the amount of dilution that the raw sewage or fecal material undergoes. It will be noted that the results at twelve and twenty-two miles show a considerable variance in favor of colon bacilli being less frequently found in the same amounts of water at the greater distance. The cause of this decrease does not seem easy of explanation, for the reason that the natural influences which tend to produce disinte-

gration of organisms as worked out and recorded by Jordan do not seem to be present in this clear, shallow, rapidly running stream, having a bed largely composed of rock.

Agitation would not seem accountable for the result, for the reason that samples collected immediately above and below Niagara Falls failed to reveal any difference in the number of organisms present. It would seem to the writer that sunlight is the only remaining natural factor that could possibly be considered, and the reduction may be due to this cause. The land on either side of the Niagara River is subject to constant cultivation, and, as many of these samples were taken during and following heavy rainfalls, it would seem, if the cultivation of lands in the near vicinity supplies any great amount of colon bacilli to a stream of this character, that the relative numbers of coli would have been materially increased at such times. As a matter of fact, this was not the investigator's experience. The number of coli present in the amount of water was materially lessened following rainfalls. This, of course, might be due to the great dilution produced by the rainfall. As judged by the investigators, the relative amount of colon supplied, if any, must have been extremely small to permit of the reductions noted. As a recapitulation of the results of the second division's work, the following conclusions would seem justifiable:

1. The presence of colon bacilli in the majority of 10 c.c. lots of a sample should be looked upon as suspicious.

2. When found in the majority of 5 c.c. lots of a sample it should be looked upon as decidedly suspicious.

3. When found in 50 per cent. of 1 c.c. lots of a sample it can be considered as evidence of direct fecal pollution.

4. That whereas cultivated lands bordering on water supplies may furnish sufficient quantities of colon bacilli during certain periods to permit of their being detected when large quantities of water are examined, it does not appear that in the examination of 1 c.c. amounts of samples that colon bacilli coming from this source will be present in sufficient numbers to permit of their detection in the majority of the 1 c.c. examinations.

The third division of the work, the length of life of the colon bacillus in water under natural environment, was conducted as follows:

Three wells were found, which, after thorough inspection of the surrounding territory and careful bacterial examination, did not reveal colon bacilli. There was placed in each well one quart of excrement, the source of same being as follows:

Human in Well A, cow in Well B, and horse in Well C.

After ten days all wells were examined and colon bacilli were found in abundance, the exact number being in the neighborhood of: Well A, 500 to 800 per c.c.; Well B, over 3000 per c.c.; Well C, over 1000 per c.c.

After thirty days the number of colon in Well A were approximately the same; in Well B the colon had greatly decreased; in Well C the colon had decreased 10 per cent. After ninety days the number of colon bacilli in Well A had decreased over 11 per cent.; in Well B could be found only occasionally in c.c. quantities, and in Well C there was but an average of four colonies of colon bacilli to the c.c., counting four plates. It was impossible at this time to continue the investigation of Wells B and C, but an examination of Well A one hundred and ninety days after the introduction of excrement revealed five colonies of colon bacilli per c.c., averaging three lactose litmus agar plate. From these tests it would seem that the length of life of colon bacillus in well water under natural conditions varies with the variety. It was impossible to conduct an investigation relative to the length of life of colon bacilli in stream water. The following recapitulation of results would seem justifiable:

1. The resistance of the colon bacillus in water is influenced by the animal source of the material.

2. That there is a gradual decrease in the number of organisms where there is no additional pollution.

3. That colon bacilli in human excrement is capable of surviving at least one hundred and ninety days in well water.

The fourth division of the work, that of considering the degree of frequency with which colon bacilli can be found in water known to be polluted with sewage, is covered under the results reported in the work of the second division.

The fifth division of the work, the degree of frequency with which colon bacilli can be found in waters not presumably contaminated with fecal material, was conducted as follows:

The work of this division was mostly confined to the examination of well waters, for the reason that after a most diligent search the investigators were unable to locate in the near vicinity to Buffalo a single stream, and but one lake (Hemlock, near Rochester) from which the presence of sewage could be presumably eliminated. The source of this lake is said to be springs, and it is not immediately connected with any other great body of water. The great distance of this lake from the point where the work was conducted rendered it impossible to obtain any great number of samples for investigation. Seven samples were examined, all being collected upon the same day, at different locations in the lake, and, fortunately, at a time following a forty-eight-hour rainfall. The land surrounding Lake Hemlock for a considerable number of feet is controlled by the city of Rochester, and is protected as a water-shed to this lake. The remaining adjacent lands are used for farming purposes.

After many attempts, using 1 c.c., 3 c.c., 5 c.c., and 10 c.c. lots from each of the seven samples, it was impossible to detect the presence of colon bacilli. The well-water tests included, on an

average, four examinations of two different samples from thirty-one different wells. 5 c.c. was the amount selected in each instance. None of the examinations revealed the presence of colon bacilli.

A recapitulation of the results of the five divisions of the work seems to justify the following conclusions:

1. That there is a difference between the bacillus acidi lactici of Hoeppe and the colon bacillus.

2. That presumptive tests, although of unquestionable value as primary procedures, and serviceable for prolonged routine test of a supply, where the analyst is familiar with all conditions and can ascertain at a glance any variable feature, must not be relied upon in arriving at a positive definite diagnosis of the colon bacillus.

3. That the colon bacillus cannot be constantly detected in c.c. amounts of water from the same source, although it may be heavily polluted with sewage.

4. That the presence of colon bacilli in 50 per cent. of c.c. amounts of water is strongly indicative of sewage pollution.

5. That the ordinary cultivation of farm lands, although it may be the source of some colon bacilli to a water supply, does not seem to play any great role as such, and that this source need hardly be considered when the majority of 1 c.c. samples reveal the organism.

6. That agitation has little or no destructive influence upon colon bacilli in water, and that light appears to exert a destructive influence.

7. That the positive detection of the presence of true colon bacilli in waters not presumably receiving sewage is rare.

8. That it is possible there have been organisms mistaken for colon bacilli, probably through too great reliance upon presumptive tests.

OBSERVATIONS UPON THE CHROMATIC VARIATIONS IN THE PRECIPITATED AND SEDIMENTED CHLORIDES, SULPHATES, AND PHOSPHATES OF URINE.[1]

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and

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of Chicago.

In making quantitative analyses of urine for chlorides, sulphates, and phosphates by the volumetric method, using the centrifuge for the purpose of throwing down the precipitate, certain chromatic variations in the sediment have long attracted our attention. Although

[1] Read before the Chicago Medical Society, January 6, 1904.

such variations in color were particularly noted by one of us in the earliest days of centrifugal analysis, yet no systematic record of these was made until about eighteen months ago, since which time an accurate notation covering this point has been made in every urinary analysis made in our laboratories. These examinations, numbering more than 2000, have been sufficiently numerous to warrant an analysis of the results of our observations, and these are herewith presented, in the form of a preliminary report.

The urines analyzed were from healthy persons, mainly beyond middle age, who presented themselves, as a routine, for physical examination, and from invalids of all ages and affected with a great variety of ailments. In the latter class were included cases of the acute infections, tuberculosis, carcinoma, diabetes, nephritis, anæmias, circulatory disturbances, etc. Various foods and medicaments were ingested, and these were noted. In nearly every case the twenty-four hours' urine was employed and the examinations were repeated daily or at longer intervals.

The analyses were made in the ordinary manner and included information upon the nature of the specimen, quantity in twenty-four hours, transparency, sediment, color, reaction, specific gravity, total solids, urea, chlorides, phosphates, sulphates, albumin, sugar, diazo reaction, indican, bile, hæmoglobin, casts, blood elements, epithelium, crystals, amorphous sediment, etc. The chlorides were precipitated by a 10 per cent. solution of nitrate of silver, the phosphates by the alkaline magnesium solution and the sulphates by the standard acidulated chloride of barium solution. For the purpose of estimating the color the sediment was compared with a standard chromatic scale.

The chlorides showed the greatest variations in color, and for the sake of brevity our remarks will be confined mainly to this phase of the subject.

The colors assumed by the chloride sediment varied from the purest white, through innumerable shades of yellow, orange, green, and red to black, as shown in the drawings. It is worthy of note that no two specimens were exactly alike. Thus, if two specimens, either of which would be designated as pure white, were compared, noticeable differences in shade could be readily detected.

The white sediments were more numerous than any other. These varied infinitely in shade, through pure white; white with a more or less distinct yellowish or, and oftenest, a pinkish tinge; white with a slight bluish tinge; grayish and dirty white. These in turn ran, by insensible gradations, into the drabs and slates. The yellow sediments rose up from the yellowish-white and passed on through the various shades of light yellow, canary yellow, ochre and deep yellow, losing themselves in the oranges, salmon colors, old-gold and green sediments. The reds began with the most delicate shades of pink, pale reds, yellowish reds, rose tints, wine colors to dark reds; light, dark,

yellowish, and seal browns to blacks. In two specimens a beautiful light lilac-purple color was developed. In numerous instances the colors were strikingly pure and beautiful. If the test-tube were not well shaken after the addition of the nitrate of silver solution a marbled or mottled appearance was likely to be produced.

In some instances the chromatic bodies were soluble and imparted to the supernatant liquid a coloring more or less nearly approximating that of the sediment—usually of a lighter shade. In others the supernatant liquid was colored some shade other than that of the sediment—*e. g.*, pink with a white sediment. In yet others more or less of the coloring matter was abstracted from the urine, leaving it distinctly lighter. In a small proportion of cases the supernatant liquid was unchanged in color.

The variously colored chloride sediments were compared with the color, reaction, specific gravity, total solids, total urea, diazo reaction, indican, sugar, albumin, phosphate, and sulphate sediments of the urine; with exposure of the sediment to light; with the medication, etc., without observing any constancy of relation.

For example: Although the white sediments were usually obtained from yellow urines, yet such sediments were also seen in red and even brown urines. The same applied to the yellow sediments. The peculiar and beautiful old-gold sediments were found in light yellow, yellow, yellowish-red, and red urines. The pale-green, bright-green, and dark-green sediments were observed only in yellow urines. Olive sediments were noted in variously colored urines, but were almost uniformly present in those which were bile-stained. Orange sediments were found only in red urines. Pink, light-red, and yellowish-red sediments were seen in yellow, amber, red, and brown urines. Rose-tinted and wine-colored sediments were noted in yellow, amber, and red urines. A single lilac sediment was encountered in an amber urine. The variously shaded brown sediments were usually observed in red urines, but in a few instances were seen in yellow urines. The brownish-black and black sediments were usually met with in light-yellow and yellow urines, rarely in amber and red urines.

In one notable case of chronic interstitial nephritis, in which the urine has been habitually a very light yellow, the sediment was, for several years, regularly dark brown or black. Recently, without recognizable cause, it has changed to a dirty white or gray color.

In comparing the colors of the chloride sediment with the specific gravity of the urine it was noticeable that the average specific gravity diminished as the colors darkened, but very low and very high densities were observed in every group of color shades. The opposite, with like exceptions, applied to the lighter shades of color and the moderate and higher ranges of specific gravity. Similar statements may be made regarding the relations existing between the urea and color of the sediments.

The presence in the urine of albumin, of sugar, of indican, of the diazo reaction, etc., were without apparent influence, and this could be said of the medication observed, especially with reference to salol, guaiacol, acetanilid, salicylic acid, morphine, iron, mercury, iodide of potassium, etc.

The bulk percentage of the chloride sediment, which varied from a mere trace to 50 per cent., appeared to have no bearing upon the color. It is true, however, that in some groups of colors—*e. g.*, the wine-colored sediments, the percentages were uniformly low, while in others, as note the pink sediments, they were as uniformly high.

The color of the chloride sediment was independent of the action of light upon the precipitate, before and after sedimentation. When exposed to light it underwent, upon the surface, the changes which are usual with solutions of nitrate of silver in the presence of organic matters, but this had no connection with the phenomena which we observed.

The colors of the phosphate and sulphate sediments bore no close relation to those of the chlorides. They were usually some shade of white or fawn color. We might say that the phosphates were oftenest of a pure white color, or of a delicate fawn or buff color, while the sulphates were oftener of a dirty white or buff color. It rarely occurred that these were of any other color where the chlorides were white or light in color. On the other hand, the chloride sediment might have shown any of the darker colors, even black, while the phosphates and sulphates remained white or light in color.

In many instances these sediments appeared in a variety of colors —*e. g.*, pinks, light browns, yellows, drabs, etc., rarely in the darker colors. In some cases striking colorations were noted. In one specimen the chlorides were black, the phosphates yellow, and the sulphates orange. In another the chlorides were seal brown, the phosphates orange, and the sulphates green. In yet another the chlorides were dirty white, the phosphates a beautiful pink, and the sulphates a bright, deep yellow.

In conclusion we will say that no reasonable explanation is offered or known to us for the phenomena observed. We have been unable, as yet, to find the key to the situation. That these chromatic variations in the sedimented chlorides, phosphates, and sulphates depend upon more or less important vital processes, most probably in the intestines, and of a fermentative or putrefactive nature, we believe to be true. We are of the opinion, also, that a clear understanding of this subject would probably be of diagnostic importance. For this reason we have thought it best to present our observations at the present time, with the hope that by attracting attention to the subject the solution of the problem may be expedited.

EXPERIMENTAL STUDIES ON THE ETIOLOGY OF ACUTE PNEUMONITIS.*

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Introduction.

Acute exudative inflammation of the lungs may develop as a metastatic lesion secondary to disease processes in other parts of the body, or it may accompany acute interstitial processes arising usually from the pleura, or it may arise as a primary infection of the lung forming patchy bronchopneumonic or diffuse lobar lesions. The bacterial incitants of acute primary infectious processes in the lung are now well known. Our knowledge of the essential conditions which determine the extent and nature of the disease processes in the lung and elsewhere, however, lacks the precision which can come only from exact experimental data. This may be attained only when it is possible to reproduce at will the various disease processes in animals. With pneumococcus pneumonia this has not heretofore been satisfactorily accomplished. As a result of a long series of experiments, I have finally determined a method by which the diffuse lesions of pneumococcus pneumonia may readily be incited in the rabbit. This method it is the purpose of this paper to record; but the failures and successes of others have in such large measure contributed to my final results that they may with advantage be briefly considered. The significance of this previous work, however, may not be fully appreciated without summing up our knowledge of the distribution and disposal of bacteria in general in the respiratory apparatus, of the bacterial incitants of pneumonia, and of the paths of infection.

Bacteria of the Normal Respiratory Apparatus. Inspired foreign particles and bacteria, as shown by the researches of Arnold[2] and many others, are deposited chiefly on the moist surfaces of the upper respiratory passages, although they may occasionally be carried to the alveoli of the lung. For most bacteria the healthy mucous membrane is an unfavorable environment, yet this varies greatly in different parts of the tract and with different species of bacteria. In the *mouth* and *nares* bacteria are being constantly deposited on the mucous membranes. As indicated by the researches of Thomson and Hewlett,[178] Wright,[197] Nenninger,[131] Müller,[126] and Laschtschenko,[109] some of them disappear very rapidly; others may develop and exist as harmless parasites. These secretions thus contain

* Read in abstract before the American Association of Pathologists and Bacteriologists, April, 1903.

many different species of micro-organisms, among which the bacteria commonly associated with pneumonia—the pneumococcus, streptococcus, staphylococcus, and the bacillus of Friedländer—have often been found. Suffice it to note that the pneumococcus was present in a large proportion of Sternberg's cases,[173] 20 per cent. of Fraenkel's cases,[67] 17 per cent. of Besser's cases,[17] 20 per cent. of Wolf's cases,[196] 30 per cent. of Bein's cases,[15] 55 per cent. of Miller's cases,[123] 4 per cent. of Neumann's normal cases,[136] and in 100 per cent. of the forty tonsils examined by Bezancon and Griffon.[20] Netter[132] divided his cases into those with and those without a history of pneumonia, and found the pneumococcus in four out of five and in one out of five cases, respectively, and he also claims to have found the organisms virulent five, ten, or more years after a pneumonic infection. Furthermore, it is significant to note that it has been experimentally shown by Guarnieri,[80] by Bordonni-Uffredozzi,[24] by Grawitz and Steffen,[77] by Spolverini,[170] and by Ottolenghi[138] that the pneumococcus in sputum may remain alive and virulent for two to four months.

In the *trachea* bacteria are also deposited on the mucous membranes,* but under normal conditions these are comparatively few in number and are rapidly disposed of by the cilia, and also by the action of the mucus, which, in the researches of Wurtz and Lemoyez[198] with sputum, of Walthard,[187] of Stroganoff,[175] and of Morisani[124] with the uterine secretions, and more recently of Arloing[2] with pure mucus, has shown marked bactericidal qualities.† Examination of the human trachea at autopsy, as in the studies of Baumgarten,[10] Hoffmann,[91] v. Besser,[10] Ritchie,[152] Claisse,[38] and Durck,[45] has revealed the presence of micro-organisms in a considerable proportion of the cases, but the trachea and lung at autopsy, although of normal appearance, may not be considered to be under normal conditions. Normal conditions, it is evident, are more closely approximated in the researches conducted on animals, as in the studies of Hildebrandt,[89] Klipstein,[102] Gobell,[74] Rosenthal,[154] Beco,[12] Buttersack,[30] Boni,[23] Barthel,[9] and Calamida and Bertarelli.[31] In these examinations of the trachea of animals, bacteria have not often been found, and the lower portions of the trachea and the bronchi have thus been considered to be practically sterile.‡

* As suggested by the researches of Slawjansky[167] and of Kuttner[107] with the injection of foreign substances, and of Pernici and Scagliosi[143] with the injection of bacteria into the general circulation, the possibility of bacteria being carried to and through the mucous membrane from the circulating blood may also be considered.

† In the experiments of Grawitz,[77] Steffen, [77 171] and also of Hopkins[92] this action of mucus was not detected in sputum sterilized by heat.

‡ In the course of my experiments, examination of the lower portion of the trachea clearly indicated that in the rabbit, at least, this portion of the respiratory tract is normally free from micro-organisms; but that contaminations, attributed very largely to the death agony, readily occur; and that the bacteria of such contaminations may grow so that, unless the animal be examined immediately after death, considerable numbers of bacteria may be found. Furthermore, animals dying of disease, when compared with those killed, frequently showed the presence of contaminating bacteria in this portion of the respiratory apparatus, although the entire tract was apparently normal.

In the normal *lung* bacteria do not, so far as is known, exist as harmless parasites. The researches of Prudden and Northrup,[144] Tschistovitch,[180 181] Grammatschikoff,[75] Silfast,[165] and others show that pathogenic as well as non-pathogenic bacteria in the air spaces degenerate: some are taken up by the phagocytes and carried into the lymph channels; others are destroyed by the body fluids. By these processes considerable numbers of bacteria may be disposed of in a comparatively short time.

Bacterial Incitants of Pneumonia. The infectious nature of pneumonia was first definitely established by the researches of Friedländer,[71] Talamon,[176] and Fraenkel.[67] The various studies of the pneumonic lung at autopsy in long series of cases by many subsequent observers, notably, Weichselbaum,[190] Wolf,[190] Finkler,[62] Prudden and Northrup,[144] Kreibach,[105] Netter,[133 135] Pearce,[141] Durck,[44] and Howard,[93] have served to indicate the etiological importance of the different bacterial incitants. The pneumococcus is now considered as practically the sole incitant of the diffuse lobar lesions. Netter believes the disease to be specific; others concede a small percentage of the lesions to the bacillus of Friedländer. In bronchopneumonia the more recent researches indicate that the pneumococcus rather than the streptococcus is more frequently the incitant, yet in the secondary lesions following certain of the exanthemata the streptococcus is still considered the more important.

Although the inflammatory reactions induced by the pneumococcus, streptococcus, staphylococcus, and pneumobacillus are somewhat similar, they differ in many respects, so that there are certain types of lesion more commonly associated with one species than with others. The pneumococcus lesions are in general more diffuse, œdematous, fibrinous, hemorrhagic, and less necrotic than those induced by either the streptococcus or pneumobacillus. In pneumococcus lesions gangrene rarely develops, except as the result of secondary infection; on the other hand, the pneumobacillus is not infrequently associated with such a condition. The pneumococcus and streptococcus are, on the whole, more similar in their pathogenic effects than any of the others; but in the lung the streptococcus rarely if ever gives rise to the lobar form of pneumonia. The staphylococcus processes are less variable, almost always circumscribed, rarely diffuse or fibrinous, as compared with those of the other three species.

These broad differences, to some extent dependent upon the virulence of the bacterial species, may be modified by many conditions, such as the age or susceptibility of the individual, and more particularly by the susceptibility of the race or species of animal infected. In respect to infection with the pneumococcus, Behring and Nissen,[14] Fraenkel,[67] Gamaleia,[72] Kruse and Pansini,[106] and many others have determined that mice and rabbits are the most susceptible; guinea-pigs, rats, squirrels, cats, dogs, sheep, horses, and man

are in varying degrees less susceptible; and fowls more or less immune.

Paths of Infection in Pneumonia. Infection through the air-passages is undoubtedly the rule in bronchopneumonia; but certain secondary pneumonias arising by hæmatogenous infection may so closely simulate bronchopneumonia that the rule must either be excepted for these cases or they must be classified with the metastatic pneumonias. Most observers believe that lobar pneumonia also develops from an infection through the air-passages; but regarding the universality of this there is some question, doubtless arising from the unsatisfactory results that have attended tracheal inoculations in animals and other similar experimental attempts to induce the lobar lesion. Two other paths of infection, the hæmatogenous and the lymphatic, have therefore been considered by some theoretically possible. As supporting hæmatogenous infection, the results of the blood examinations of pneumonia patients have been cited. Careful scrutiny of these, however,* reveals the fact that while bacteriæmia develops early as well as late in the disease, there is no indication that this is other than secondary to the local lesion. The occurrence of pneumonia in the fœtus offers the clearest example of hæmatogenous infection. Cases of such infection have been reported by Strachan,[174] Marchand,[117] Thorner,[179] Netter,[134] Viti,[184] Czmetscha,[41] and Delestre.[42] These reports, however, are in many respects inadequate; in some histological examinations of the lesions were not made, in others infection by the air-passages after birth could not be excluded. They, therefore, fail to establish the occurrence of lobar pneumonia from placental infection. Experimental support of hæmatogenous infection in lobar pneumonia is certainly very meagre, uncorroborated, and relatively insignificant. Finally, suffice it to note that, clinically as well as experimentally, pneumonic lesions of the lobar type are uncommon in races or individuals very susceptible to systemic pneumococcus infection and more common in resistant individuals or species in which systemic infections are less usual.

There are few facts to support a theory of lymphatic infection. Grober's[79] interesting work on the tonsil and its lymphatic connections is extremely significant as applied to tuberculous and pleural infections, but the plague bacillus is the only species which is definitely known to reach the lung through the cervical lymphatics and give rise to an acute exudative pneumonitis. These plague pneumonias, however, are of a peculiar metastatic lymphatic type, quite different from the lobar lesions.

In view of these facts and in the absence of reliable positive data,

* Witness, for example, the studies of Guarnieri,[80] Fraenkel,[67] Banti,[8] Belfanti,[16] Sittmann,[166] Sello,[164] James and Tuttle,[95] Prochaska,[145] White,[193] Baduel,[7] Pane,[130] and Wandel,[189] many of which, and others not cited, have been reviewed recently by Ewing.[60]

the possibility of lobar pneumonia arising by hæmatogenous or lymphatic infection must be considered as not yet established.*

Previous Researches on Experimental Pneumonia.

The earliest attempts to induce pneumonia in animals, which were made when the disease was attributed to exposure or fatigue and before its infectious nature was determined, are now chiefly of historic interest. The first significant experiments comprised the inoculation of animals with the exudates and autopsy material from pneumonia cases. After the infectious nature of the disease had thus been established and the several bacteria concerned isolated and differentiated, greater scope and precision of experimentation became possible, pure cultures replaced the exudates, etc.; or if the exudates were used the bacteria contained in the exudates were previously determined, and special methods of inoculation were adopted. At first the lungs were inoculated through the chest-wall, then this rather crude method was discarded and the animals were forced by various contrivances to inhale the infectious material. Finally, tracheal injections of the infectious material were used. Although infection of the normal lung of various animal species were not infrequently secured by certain of these methods, typical diffuse pneumonic lesions rarely developed. Attention was therefore directed to the animal and attempts were made through injury to render the lung more susceptible to infection. The results of these experiments as regards the development of circumscribed bronchopneumonic types of lesions were more satisfactory and uniform; but as regards the development of diffuse lobar types of lesion were uncertain and far from satisfactory.

The experiments of former observers may, therefore, be divided into two main classes: those on normal and those on artificially predisposed animals.

Previous Attempts to Induce Pneumonia by Infection of the Uninjured or Normal Lung. *Intravenous*, *subcutaneous*, *intraocular* inoculations—in short, all methods giving rise to a primary general infection, whether practised in the ordinary laboratory routine or in the hope of securing pneumonic lesions—have, with a few uncorroborated exceptions,† uniformly failed to give rise to the

* This, however, does not exclude the possibility of a metastatic pneumonia, as has been exceptionally noted, simulating the diffuse lobar processes. In fact, between the more typical processes of all forms of acute exudative pneumonitis intermediate lesions occur which histologically are distinguished with difficulty.

† Schultz[103] reports pneumonic lesions in eight out of fourteen rabbits inoculated intravenously with pneumococci. Apparently the collapsed lungs were examined, and certainly the lesions found were inaccurately described as typically exudative. Klipstein[104] reports one instance of a diffuse pneumonia being found after subcutaneous inoculation with a colon bacillus, and Fraenkel[66] noted the exceptional development of pneumonic lesions after subcutaneous inoculation of the thorax with the pneumococcus. An early observer, Klebs,[100]

definite lesions of either bronchopneumonia or lobar pneumonia. *Intraperitoneal* inoculation has similarly failed, the few exceptional lesions being of the pleuropneumonic type.

With *intrathoracic* inoculation the needle may or may not penetrate the lung; if the lung tissues are entered a local injury, with more or less hemorrhagic extravasation, results; if not, the pleural cavity only is inoculated and the infection of the lung is secondary, thus pleuropneumonia is incited. By intrathoracic inoculation of pneumococci, Talamon,[176]* in eight out of twenty rabbits, Weichselbaum[190] rarely, Gamaleia,[72] in dogs and sheep always, obtained pneumonic lesions, some of which were described as diffuse and lobar in type. With the pneumobacillus, Friedländer,[71]† in thirty-two mice and in one out of four dogs, Weichselbaum,[190] occasionally in mice and rabbits, obtained pneumonic lesions. In other similar experiments of these and many other observers, notably Kruse and Pansini,[106] Fraenkel,[67] Salvioli,[157 158] Foa and Rattone,[66] Klein,[101] Sternberg,[172] v. Besser,[19] and Silfast,[165] with pneumococci, streptococci, staphylococci, and the pneumobacillus, conducted on mice, rabbits, guinea-pigs, dogs, and horses, the inoculation failed to give rise to pneumonic lesions, although in the very susceptible animals a general systemic infection often ensued.

The *inhalation* of infectious material has been used chiefly as a test of the permeability of the normal lung to bacteria; but owing very largely to changes occurring in the virulence of the bacteria as a result of cultivation or the drying and pulverizing, and to the uncertainty as to how much if any of the infectious material ever reaches the air spaces, inhalation has proved a most uncertain method of infecting the lung. Pneumonic lesions usually circumscribed have, nevertheless, in exceptional instances, been noted, as in the researches of Buchner, Merkel, and Endelen,[29 54] Eppinger,[55] and Grammatschikoff,[75] with anthrax; of Friedländer,[71] Emmerich,[51]‡ and Chester,[36] with the pneumobacillus; and of Silfast,[165] with streptococci. Weichselbaum[190] failed to secure pneumonic lesions in his experiments with inhalation. The inhalation of the plague bacillus, as in the experiments of Batzaroff[11] and others, doubtless owing to the extreme virulence of this organism and the susceptibility of the animals used, has been remarkably successful in giving rise to the different types of plague pneumonia.

reports the development of pneumonic lesions after intraocular inoculations with exudates which were not obtained in Veraguth's[183] similar experiments. In the course of my experiments, I have occasionally found at autopsy extensive consolidations of the lung, in which no bacteria or bacteria other than those inoculated were present, and which could only be attributed to chance or an intercurrent infection. A similar undetected infection may account for some of these unusual findings, especially in the early researches.

* Exudates were used for inoculation.

† Identity of cultures used is somewhat doubtful.

‡ Emmerich[52 53] claims to have invariably secured typical diffuse lesions in animals which had inhaled virulent pneumococci. His observations have never been corroborated; in fact, such inhalations have usually proved harmless.

By *tracheal injection* of the infectious material greater precision was given to the experiments and more definite results were thereby attained; but the virulence of the different bacteria in these experiments, as in those with inhalation, was a most important and variable factor. With pneumococci introduced in this way, Fraenkel[67]* rarely, Salvioli[159] in one rabbit and in two of four guinea-pigs, Kruse and Pansini[106] in possibly one of twenty-eight dogs, Tschistovitch[181] in seven of nineteen cats, and exceptionally in rabbits, obtained diffuse pneumonic lesions. Similar experiments of these and other observers, notably, Gamaleia,[72] Klein,[101] Guarnieri,[80] Griffiini and Cambria,[78] Talamon,[176] Lipari,[112] Welch,[191] Arustamow,[4] Müller,[125] Aufrecht,[5] Durck,[46] Coco and Drago,[39] and Carnot and Fournier,[33] with pneumococci, conducted on rabbits, guinea-pigs, cats, dogs, and sheep, failed to give rise to typical lesions, the inoculation proving either harmless or, as in very susceptible animals, giving rise to systemic infection, usually without, but in some instances, with small circumscribed lung lesions.

Patchy or circumscribed lesions have been occasionally induced by the tracheal injection of other bacteria, as in the experiments of Prudden and Northrup,[144] Orloff,[127] Fleck,[65] Laehr,[108] Durck,[46] Silfast,[165] and Beco,[13] with streptococci and staphylococci; of Lépine and Lyomet[111] with the typhoid bacillus; of Gamaleia[72] and of Tschistovitch[180] with the chicken cholera bacillus; and of Tschistovitch[180] with the bacillus of rouget du porc. Diffuse lesions following endotracheal inoculations have been reported by Gamaleia[72] with the bacilli of anthrax and chicken cholera, and by Bosc and Galavielle[25] with the micrococcus tetragenus. Finally, the various forms of plague pneumonia have been frequently induced by this method of inoculation. These are often hemorrhagic, usually bronchopneumonic, sometimes confluent and diffuse.

Experiments on the normal animal having given unsatisfactory results, attempts were made to render the lung more susceptible to infection by means of predisposants, which may be considered as acting chiefly upon the lung locally or upon the system at large. Many conditions, such as the inspiration of irritating substances, exposure to cold, trauma, fatigue, and disease, have long been recognized clinically as favoring the development of pneumonia in man. These and other conditions used as experimental substitutes for them have been extensively studied as to their effect *per se* on the animal and when combined with inoculation.

Previous Attempts to Induce Pneumonia in the Locally Predisposed Animal. The early researches of Heidenhain,[84] Arnold,[3] and Massalongo,[119] and the more recent work of Klipstein[102] and Beco,[13] in which the lungs of animals were exposed by inhalation or injection to various noxious substances in gaseous, liquid, or

* More often with attenuated than with virulent cultures.[60]

solid state, suffice to show that a series of changes largely desquamative, but often exudative, are effected in the tissues of the lung by these irritants.* That the changes thus induced in the lung tissue favor infection and the formation of lesions is well shown by the numerous experiments in which the injured lung has been directly inoculated through the trachea or the predisposed animal has been forced to inhale the infectious material. Such are the experiments of Buchner, Merkel and Enderlen,[29] and Muskatbluth[127] with anthrax; and of Prudden and Northrup,[144] Silfast,[165] and Beco[13] with streptococci and staphylococci; but the lesions in these experiments were usually circumscribed and bronchopneumonic in type. Typical diffuse lesions, however, Gamaleia[72] claims were always obtained when the injured lungs of resistant animals, such as the dog and sheep, were inoculated through the trachea with virulent pneumococci; in the normal lungs of these resistant animals the inoculation proved harmless, in the more susceptible animals this injury merely favored the development of fatal bacteriæmia without lung lesions.

As a result of *trauma* the lung tissues may be injured and thus predisposed to infection. If the integrity of the thorax is destroyed and the lung thereby exposed to external contamination, a wound infection accompanied by various disease processes of the lung, as well as of other tissues, may develop. If, on the other hand, the thorax remains intact, the trauma, acting purely as a predisposant, may give rise to changes in the lung, such as have been noted experimentally by Reineboth[146 148] and others,† which may favor the development of infectious material carried to the lung by the usual channels. In experimental pneumonia trauma is obviously a constant and possibly a determining factor.

Exposure to *cold*, long considered an all-important factor in the development of pneumonia, is now classed with trauma as a predisposant,‡ which, only in certain cases, may be a determining factor.§ Experimentally the effect of exposure to cold has been extensively studied. The changes brought about in the animal tissues have been attributed to the retention of deleterious products

* Extensive lesions closely resembling those of acute exudative pneumonitis have been secured by such treatment without bacterial agency, but this is exceptional and the reports are confined to a few of the earlier observers.

† Traumatic pneumonia has also been extensively studied by Litten,[113] Meunier,[121] Reynaud,[150] Souques,[168] Gauthier,[73] and Schild.[161]

‡ Witness, for example, the table compiled by Comby :[40]

Bouilland attributed to cold	. . . . .	75	per cent.
Grisolle	" "	20	"
Ziemssen	" "	9	"
Jurgenson	" "	4	"
Griesinger	" "	2	"
Massalongo	" "	0	"

§ Ruhemann,[155] however, considers the exposure to cold the exciting factor, and the presence of the bacteria the predisposing factor in the etiology of pneumonia.

of the body metabolism from diminished excretion (Eisenmann[50]), to reflex nervous action (Heymann[88]), and to the direct action of the cold on the tissues (Rosenthal[155]). These are very largely dependent upon the nature and extent of the exposure, upon the animal species used, and as shown by the researches of Nasaroff,[120] Durig,[47] and Lode,[115] upon the nutritive condition of the individual exposed. As a result of exposure the body temperature may be greatly influenced, as in the experiments of Eve,[59] who found that the experimental extremes compatible with recovery approximate those clinically observed in man, viz., 45° C. (113° F.) and 25 C. (77° F.). The marked fluctuations in blood pressure following exposure to either heat or cold, as in the experiments of Hegglin,[83] Grawitz,[76] Hermann,[87] Hadl,[81] and others, may give rise to hyperæmia, congestion, transudation, or even hemorrhage. Marked anæmia,* with reduction of both cells and hæmoglobin and with hæmoglobinuria, may develop, as in the studies of Chvostek,[37] Erhlich,[48] Grawitz,[79] Ebstein,[49] Fischl,[64] and Rheinboth and Kohlhardt.[149] Other cells of the body may undergo parenchymatous degeneration, as was noted by Lassar[110] and many others since his time. That these changes in the tissues resulting from exposure to cold predispose to many infections has been established by a great variety of researches, notably the early observers, Pasteur,[140] Wagner,[185] Ernst,[56] and Sawtschenko,[160] and the more recent writers, Chelmonski,[35] Lode,[114] Dieudonne,[43] Silfast,[165] Sanarelli,[159] Kisskalt,[99] and Reineboth and Kohlhardt.[149]

Owing to the anatomical structure of the lung these circulatory disturbances and the changes dependent upon them are especially well marked in this organ. Thus, in exposed animals, extensive lesions of the lungs were noted as early as 1862 by Walther,[188] and in 1870 by Wertheim,[192] and also recently by Durck.[45] The development of pneumonic infection in animals exposed to cold has been studied by means of the tracheal injection or the inhalation of infectious material, as in the experiments of Lode[114] and of Platania,[142] with the pneumobacillus and staphylococcus; of Silfast,[165] with streptococci; of Beco,[13] with staphylococci; of Carrière,[32] with attenuated pneumococci; and of Lipari,[112] with virulent pneumococci. In these experiments infection developed, and lesions, usually circumscribed or bronchopneumonic, were obtained more frequently than in normal animals. Lipari[112] alone reports definite results. Diffuse lobar pneumonia was obtained in all the exposed, but in none of the normal, rabbits of his experiments.

Circulatory changes, whether purely reflex and evanescent or associated with definite lesions and damage to the tissues, have been considered determining factors of local predisposition in the lung

* The stimulating effect of mild exposure to cold has long been recognized, and the blood as well as other tissues may be greatly benefited by such exposure, as in the studies of v. Breitenstein,[28] Thayer,[177] Winternitz,[195] and of Speck.[169]

as in other organs and tissues. Attempts to demonstrate this experimentally have not been satisfactory: thus, Buchner[28] concluded that arterial hyperæmia was salutary; Kisskalt,[98 99] that arterial hyperæmia favored infection, but that stasis hyperæmia, as in tuberculosis, may act differently; Frenkel,[70] that sensory paralysis increased the susceptibility, while vasomotor paralysis increased the immunity, but neither had any effect in determining the general infection. Other observers, notably, Hermann,[86] Kasparek,[97] Meltzer,[120] Nekam,[130] Charrin and Ruffer,[34] and Roger,[153] have obtained results which suggested that innervation of a part favored the development of infection. These uncertain results are obviously to be attributed to many variable and indeterminate conditions, relating chiefly to the susceptibility of the animal, on the one hand, and to the nature and virulence of the bacteria on the other.*

The normal lung, however, as compared with the other tissues and fluids of the body, is such an unfavorable environment for bacterial growth that a hyperæmia, with transudation by creating a more favorable soil, may be theoretically considered to favor infection in this organ. For experimental support of this, suffice it to refer to the above-noted predisposing action of irritation and trauma and of exposure to cold, the effects of which in the lung are largely due to circulatory changes.

The so-called *vagus pneumonias* have been studied by many of the early investigators, by Schou,[162] and recently by Müller[125] and by Esser.[58] Section of the vagus nerve, on one or both sides, has been frequently followed by the development of pneumonia, which has usually been of the patchy, bronchopneumonic type, though occasionally diffuse. The paralysis of the larynx, which facilitates infection of the lung by bacteria contained in the secretions of the upper respiratory passages and the circulatory changes set up in the lung, are the main factors in these experimental pneumonias. The results of these experiments prove that the method is uncertain, and, as compared with the direct inoculation of the lung with pure cultures of accurately determined bacterial species, such procedures are obviously crude.

Clinically, *previous disease processes*, especially those of the respiratory apparatus, are said to precede the development of pneumonia, and experience has shown that such inflammatory processes not only impair the protective resources of the parts, but afford favorable conditions for an increase of virulence in the bacteria present in the secretions. In Esser's[57] experiments the permanent changes left by healed inflammatory processes also favored the development of infection, and Aufrecht[6] cites statistics to show that the primary pneumonia predisposes to subsequent pneumonic infec-

* If the circulating blood is a favorable environment for the growth of the bacteria, a hyperæmia obviously favors infection; if unfavorable, retards infection. The experiments in this field have thus as yet added but little to our general theoretical knowledge.

tions. The predisposition effected by disease processes in other parts of the body, except possibly the heart, is obviously the result of an increased general susceptibility of the individual.

Previous Attempts to Induce Pneumonia in the Systemically Predisposed Animal. Many conditions influencing the system at large are well-known predisposants to infection. Some of these are clinically known to favor the development of pneumonia, and certain of the substances or conditions used as local predisposants undoubtedly act to some extent on the general system. Special methods of securing a systemic predisposition, however, have not been used in the experimental study of the etiology of pneumonia, except indirectly by Kaminer,[96] in his work on fibrin formation in the lung. Kaminer obtained pathological changes in the lungs of rabbits poisoned by phenylhydrazin in small repeated subcutaneous doses. In one animal a diffuse fibrinous lesion was found in the lung at autopsy. Bacterial examination failed to reveal micro-organisms.

Summary of the Results of Previous Researches on Experimental Pneumonia. General systemic infection of the animal by intravenous or by subcutaneous inoculation, whether practised on the normal or on the predisposed animal, has uniformly failed to give rise to pneumonic processes. Local infection of the lung from the inhalation of infectious material or by inoculation with virulent bacteria through the chest-wall, or, preferably, through the trachea, has, in some instances, been followed by the development of pneumonia. Practically all the various forms of primary acute exudative pneumonitis have thus been occasionally induced in predisposed and even in normal animals by many different kinds of bacteria. Of the different forms of pneumonia the bronchopneumonic or patchy has been most commonly incited; the typical diffuse lobar lesions have been secured with great difficulty and exceptionally.

It is evident and was early recognized that the nature and virulence of the bacteria inoculated were extremely important factors in each experiment; but it does not alone suffice to secure infection of the lung by means of highly virulent cultures, for this may, and does, as a rule, in susceptible animals, lead to a general fatal bacteriæma, which in nowise contributes to the development of local processes. A precise experimental control of subtle relationships between the virulence of the micro-organism, on the one hand, and the susceptibility of the animal, on the other, should therefore be sought. The virulence of the micro-organisms may be, and has been in many previous experiments, controlled by passing the cultures through animals of the species to be experimented upon. The susceptibility of the animal, however, has not been so definitely kept in hand. The various grades or conditions of susceptibility were not accurately determined and cannot be precisely compared, however suggestive in theory they may be.

The Writer's Researches on Experimental Pneumonia.

My studies were undertaken with a view of determining accurately the effect of increasing or diminishing the virulence of the incitant upon the development of pneumonic infection in normal animals and in animals whose susceptibility, local and systemic, was definitely increased. By using one micro-organism, the pneumococcus, and carefully controlling its virulence, and one animal species, the rabbit, whose susceptibility to pneumococcus infection was well known, it was hoped that comparison of the results obtained in a series of systematic researches would lead to more precise methods, and thus to more uniform and certain results.

Technique. The media used for growing the pneumococci were made from meat infusion and were brought to a final reaction of less than 1 per cent. acid,* phenolphthalein being the indicator. Although glucose proved a valuable addition to the media, it was rarely used, as these cultures were very short-lived, probably on account of the acid developed. Ascites fluid was, in some instances, added to the broth. In tubes of pleuritic fluid, heated until semi-solid, although still transparent, the pneumococcus stock cultures were kept at a temperature of about 10° in an accessible form, alive and virulent for several (eight or more) months. By this means the changes in the biological state of the micro-organism that usually attend repeated transfers were largely eliminated. It was, therefore, possible to work with the same unmodified races of pneumococci in all the experiments.†

Two races of pneumococci were used, one of low, the other of high virulence for rabbits. The first (A) was isolated from a fatal case of lobar pneumonia. The virulence of this organism may be approximately suggested by the fact that intravenously inoculated, 1 c.c. of a twenty-four-hour broth culture proved fatal; injected through the trachea this dose was harmless; subcutaneously inoculated, 0.5 c.c. of a twenty-four-hour broth culture induced an abscess at site of inoculation in two rabbits, and fatal septicæmia in two others inoculated from the same culture tube. The second (B) was obtained, through the kindness of Dr. Alexander Lambert, from the laboratory of the New York Health Department, where, by repeated serial inoculation in rabbits, it had been brought to a high virulence, 0.00001 c.c. of a twenty-four-hour serum broth culture at one time proving fatal to the average rabbit. This culture had, however, lost some of its virulence, for I found that although 0.1 c.c. of a twenty-four-hour broth culture intravenously inoculated excited severe reactions in rabbits, these were not always fatal. Owing to

* A reaction of 0.5 per cent. acid, which Dr. T. C. Janeway in some unpublished experiments has found to be an optimum, was in most instances used.

† For a more complete account of this method and media, see the Proceedings of the New York Pathological Society, April, 1903.

the previous adaptation of this race to rabbits, the potential strength of the culture was perhaps greater than was represented by my figures.

The inoculations were made with a Koch syringe into the ear vein or through the soft parts between the tracheal rings into the lumen of the trachea, which had previously been exposed by an incision through the skin and fasciæ. By careful technique in operating infection of the wound was avoided. The culture fluid was directed to the left lung by elevating and tilting the animal, but forced inspirations of the fluid carried it, in some instances, to the right as well as to the left lung. At the autopsies cultures and smears were usually made from the heart blood, trachea, and liver; in addition, the pleuræ were often, the spleen and kidney sometimes, examined. The smears were stained by the Welch[191] method for staining the capsules and also by the newer methods recommended by Hiss.[90] The lungs were distended with alcohol and all the specimens were hardened in this fluid. Sections of the lung, liver, spleen, and kidney were stained and examined for bacteria by the Gram-Weigert method. Other methods were also used in special instances, and by some of these, as yet not carefully determined, capsules could be demonstrated on the pneumococci in the sections of the lesions.

Scope of the Experiments on Normal and Predisposed Animals. Intravenous, subcutaneous, and intrathoracic inoculations with pneumococci of varying grades of virulence were made in normal and in predisposed animals, with a view of retesting and corroborating the results similar methods had given in other hands. A number of tracheal injections with pneumococci of varying degrees of virulence were made in normal animals with the same object in view. The series of researches on predisposed animals with tracheal injections were thus accurately controlled. The predisposition was secured in three ways: the systemic susceptibility was increased by a chronic phenylhydrazin poisoning; the lung was locally injured by exposure to severe cold; and finally, by combining the two methods, a predisposition both local and systemic was obtained. In sets* of parallel experiments the effect of these forms of predisposition upon the development of pneumonic infection was studied by the tracheal injection of pneumococci of low and of high virulence.

Attempts to Induce Pneumonia in the Uninjured or Normal Rabbit. *Subcutaneous, intravenous,* and *intrathoracic*† inoculation of normal animals with pneumococci of varying grades of virulence failed to give rise to exudative pneumonia. *Tracheal injection* of

* Each set comprised three rabbits, not including the controls.

† Of fifteen normal rabbits, four cats, and one guinea-pig, inoculated through the right chest-wall, one cat developed a typical but small area of diffuse pneumonitis. The lungs of the other animals were comparatively free from lesions, although all the rabbits and the guinea-pig died, and local processes were found in the pleura and pericardium.

these organisms, however, yielded variable results. Pneumococci of low virulence when injected through the trachea had practically no effect on the lung and were rapidly disposed of. More virulent organisms incited varying, but for the most part small, central areas of exudative pneumonitis: of seven animals inoculated by the trachea, four died, and in two of these typical and extensive lesions of diffuse pneumonitis were found at autopsy. Pneumococci of still greater virulence injected through the trachea of five normal rabbits incited fatal bacteriæmic infections, with small areas of central broncho-pneumonitis in but two. Thus in my experiments on normal animals, as in those of other observers, the diffuse lesions of exudative pneumonitis were rarely incited, and only when pneumococci of just the requisite grade of virulence were injected through the trachea; higher grades inducing fatal bacteriæmias, lower grades proving harmless.

Attempts to Induce Pneumonia in the Poisoned or Systemically Predisposed Rabbit. In order to determine the effect of increasing the rabbit's systemic susceptibility upon the development of pneumonic infection, studies were made with intravenous inoculation and with tracheal injection of pneumococci of high and of low virulence on animals previously poisoned with phenylhydrazin hydrochlorate. As brought out by many researches, notably those of Heinz,[85] Kaminer,[96] Mya and Sanarelli,[128] and Lubarsch,[116] this drug in rabbits, besides many interesting but for the present purposes unimportant structural changes in the blood elements, gives rise to severe grades of anæmia of a secondary pernicious type with hæmoglobinæmia, hæmoglobinuria, and albuminuria. Various stages of parenchymatous degeneration and an œdematous condition of the tissues are also to be found in such animals.

Six rabbits previously poisoned by the repeated subcutaneous administration of phenylhydrazin in small doses were divided into two sets and injected through the trachea with pneumococci of low and of high virulence, respectively. All died in from twelve to fifty-six hours of a general bacteriæmic infection, and the only pneumonic lesion found was a small patch of exudative pneumonitis in the rabbit which lived fifty-six hours. The development of rapidly fatal general infections with little or no lung lesion in these poisoned animals, whether inoculated in the ear vein or through the trachea, and whether cultures of high virulence or of low virulence were used, shows that such rabbits are even less favorable subjects for the experimental incitement of diffuse lesions than the normal animal. The studies were then directed to the effect of increasing the local susceptibility of the lung.

Attempts to Induce Pneumonia in the Injured Lung or Locally Predisposed Rabbit. An increase in the susceptibility of the lung without much disturbance of the system at large is obviously best accomplished by means of local irritation. Such

methods have been so exhaustively studied by others and have proved, in the rabbit at least, so consistently unsatisfactory as a means of obtaining diffuse lesions that exposure to cold—another method of rendering the lung more susceptible—was adopted.

The animals were tied to trays and placed in ice baths at temperatures of 7° C. to 12° C. for five minutes. Immediately after the bath the animals were taken from the trays and wiped with towels. After these exposures various changes were noted. In the lungs large and small areas of hyperæmia and congestion, occasionally small hemorrhagic extravasations were found. The rectal temperature fell for a period of five, ten, or even twenty minutes after the bath; the lowest observed in animals which recovered was 26.5° C.

A general bacteriæmic infection without lung lesions followed the intravenous inoculation of these animals with pneumococci of varying degrees of virulence, and the exposure of normal rabbits to cold when combined with the tracheal injection of pneumococci also proved an inadequate means of securing definite pneumonic lesions. A study of the effect of combining these methods was therefore made.

Attempts to Induce Pneumonia in the Systemically and Locally Predisposed Rabbit. Intravenous inoculation as heretofore failed to give rise to local processes in the lung and similarly the tracheal injection of the more virulent pneumococci incited but little reaction* in the lungs of these animals, all three of which died of a general infection. With pneumococci of comparatively slight virulence the tracheal injection of these emaciated and exposed rabbits gave rise to extensive and diffuse lung reactions, which were considered typical and comparable to the lobar pneumonias of man in two of the three animals of the experiment.

Of these three rabbits: one died in twenty hours and developed slight bronchial reactions similar to those found in the animals injected with the more virulent organisms; another died in thirty hours, and diffuse lesions in an early stage involved the upper portion of the lower and the lower portion of the upper left lobes; the third lived four and one-half days, and at autopsy typical red and gray hepatization, macroscopically and microscopically, were found in the upper left lobe.

Summary of the Researches on Normal and Predisposed Animals. It was thus finally possible to approximate at least the balance of conditions as to the virulence of the bacteria on the one hand and on the other the special degrees of local and systemic susceptibility of the animal necessary for the development of typical diffuse lesions of the lung. With an increased susceptibility of the animal pneumococci of low virulence only could be used. More-

* One rabbit of the set of three lived sixty hours and showed more marked lesions than the others which died in twenty-four and thirty-six hours. None of the lesions were typical.

over, both the local and systemic susceptibility of the animal in varying degrees must be increased. Such a fine balance of conditions, it is obvious, might not always be easily obtained, and the practical solution of the problem had to be sought along other lines.

Heretofore, in the experiments of others and in my own described above, the predisposition was secured by methods which increased the susceptibility of the animal to infection. In the lungs of such animals organisms of sufficient virulence to incite extensive lesions gave rise to a rapidly fatal bacteriæmia, and the reaction of the body tissues was thereby generalized or inhibited, so that the local processes failed to develop. The attempts of others to obviate this early development of a bacteriæmic infection by selecting less susceptible animals for experimentation having proved uncertain and as yet impracticable, I sought a method of rendering the rabbit less susceptible to such infection. As this could easily be accomplished by immunization, my studies were directed to this field of experimentation.

Attempts to Induce Pneumonia in the Immunized Rabbit.

Preliminary Experiments. Two animals were immunized by the inoculation of non-virulent cultures of pneumococci. Their blood serum failed to agglutinate pneumococcus cultures in dilution of 1:1, and they died from the virulent tracheal injection in twelve and eighty hours. Two other rabbits were immunized by the subcutaneous inoculation of virulent pneumococci, which induced serious but not fatal local disease processes. Their blood sera agglutinated the pneumococcus cultures in dilution of 1:1, and they survived the tracheal injection. In the rabbit which died twelve hours after the tracheal injection, an early stage of an exudative pneumonitis involving the whole left lung was found at autopsy. Similarly extensive and diffuse lesions of a later stage were present in the animal which lived eighty hours. The other two rabbits recovered from the effects of the tracheal injection and were killed on the third day. Lesions of a resolving diffuse exudative pneumonia involving large areas in one animal and small, more circumscribed areas in the other were found in the lungs.

Additional researches were divided into three sets of experiments, respectively, comprising: five immunized and two normal rabbits, four immunized and three normal rabbits, four immunized and two normal rabbits. Of the thirteen immunized rabbits injected through the trachea, but one died of the infection, and of the seven normal animals three recovered from the inoculation. Diffuse and typical lesions were incited in a considerable proportion of the animals, and the processes were more marked and more frequently found in the immunized than in the normal control animals; but the difference was not sufficiently definite, and it was evident that there were certain

errors in the methods used. Obviously either the virulence of the pneumococci inoculated or the degree of immunization attained by the animals was at fault.

At first the immunization of the animals was thought to have been inadequate, but the fallacy in this was apparent on recalling the fact that many animals had died in the process of immunization, and the survivors used for the experiment, though often greatly emaciated, withstood the virulent tracheal injection. By means of a specially devised technique insuring accurate results* the blood sera of these animals was tested as to its agglutinative action on pneumococcus cells, and the results were compared with those obtained with other blood sera of better-known strength. Thus it was determined that the rabbits had attained an extremely high degree of immunization.

The cultures used for inoculation were of pneumococci grown in exudates taken from animals dying of pneumococcus infection and diluted with broth in about equal proportions. Inoculation with such cultures often failed to kill the normal rabbit, whereas cultures of this pneumococcus in broth or in normal sera by tracheal injection or by intravenous inoculation in much smaller doses ($\frac{1}{400}$ c.c.) invariably proved fatal. A similar loss of virulence in organisms grown in immune sera was noted by Metschnikoff,[122] and that this loss in virulence is only apparent, not real, was determined by the researches of Metschnikoff's pupils, Isaeff[94] and Arkharow,[1] and also by the recent studies of Walker.[186] The lack of virulence in the tracheal injections of my experiments was therefore attributed to the presence, in the exudates used for culture media, of protective substances, which, in the lungs of the immunized or even of the fresh normal rabbit, became active. In this way an effect was obtained comparable to a lack of virulence not actually existing in the pneumococci.

It thus became evident that in these researches, as compared with the first preliminary experiments, the conditions essential to the development of pneumonic processes in the rabbit had unwittingly been altered by the above-noted errors in technique; so much so in fact that the necessary balance for the formation of typical diffuse lesions was present in a majority but not in all of the immunized animals.

Final Experiments. By avoiding what in the previous experiments seemed to be the chief faults, namely, a too high degree of immunization in the animal, and a neutralization of the virulent inoculation, more complete results were expected and obtained in a final experiment on eleven immunized† and five normal rabbits.

* Fully described in a paper published in the Journal of Medical Research, 1908, vol. x., No. 2.

† Eight normal rabbits in the process of immunization received: *March* 6, 1903. 1.5 c.c of a salt solution suspension of pneumococcus cells dissolved by normal rabbit bile: subcutaneous. 10*th*. 5 c.c. sterilized broth culture of pneumococci: intravenous. 12*th*. 2 c.c. of the bile solu-

March 6, 1903. The eleven immunized and five normal control rabbits were tracheally injected with 1 c.c. of a culture of the extremely virulent pneumococci grown in normal rabbits' serum diluted with broth.

Of the five control animals, three died in forty-eight hours without lung lesions; a fourth lived four days, and a small area of exudative pneumonitis was found at autopsy. The fifth was dying on the fifth day, when it was killed, and a similar lesion of the lung was found in this animal.

Of the eleven immunized animals none died; but a few were seriously ill for twenty-four to thirty-six hours. The first set of eight were killed on the third day; the second set of three on the fourth day after the tracheal injection. The various lesions of acute diffuse pneumonitis involving considerable areas of the left lung were present at autopsy. The smallest lesion found in any of these rabbits comprised at least a quarter of the lower lobe. In one animal, however, the entire left lung, with the exception of the lowermost tip, was solid. Cross-section showed the granular appearance seen more markedly in the human lung.

Summary of the Experiments on Immunized Animals. It is evident from these experiments that in the lungs of immunized rabbits virulent pneumococci do not give rise to an early general infection, but are confined to the lung, where, if the animal be not too highly immunized, they develop, inducing disease processes comparable to the lobar pneumonia of man. In the experimental control of these conditions under which diffuse lesions may be obtained, there are but two chief variable factors to be considered—the virulence of the micro-organism on the one hand, and the degree of immunization on the other—both easily and accurately determined by the ordinary routine methods of the modern laboratory.

General Considerations.

The Histology of the Experimental Pneumonias. The type of inflammation in all the experimental lesions obtained with the pneumococcus was purely exudative and diffuse, usually with abundant formation of fibrin. All stages in the development of the reactions were present in the different lesions, and it was impossible to draw any sharp lines of distinction between the simple bronchitis and the bronchopneumonic reactions, or between the bronchopneumonias and the diffuse lobar lesions. The one merged gradually into that of the other, although the types were easily distinguished.

The leukocytes were usually numerous and particularly prominent

tion of pneumococcus cells : subcutaneous. 26*th*. 1.5 c.c. of clear salt solution extract of pneumococcus cells : intravenous.

Three normal rabbits in the process of immunization received : *March* 2, 1903. 3 c c. of a salt solution suspension of sediment from pneumococcus growth in glucose broth ; intravenous. 3*d*. 3 c.c. subcutaneous.

in the early stages of the lesion. The exfoliation of epithelium also occurred early in the process, but the desquamated cells were relatively more numerous in the later stages. Few fibrin fibrils could be found in the very early stages, but granules were often abundant. As has been noted by Kohn,[103] Hauser,[82] Bezzola,[21] and others, the fibrin developed and was more abundant in the early stages along the walls of the air spaces, and in places the fibrils could be traced from one alveolus to another. In the more advanced lesions the fibrin formation was most marked in the centre of the exudate, a clearer zone lying next the alveolar wall.*

The pneumococci were present, often in large numbers, in all the early stages of the lesions. The cocci were for the most part outside the cells. In resolving lesions the bacteria were often absent, even though large portions of the lung were involved. This was particularly noticeable in the lesions which were found in the immunized animals. Areas of irregular development gave to the lobar lesions during the early stages a patchy appearance. These areas may or may not correspond with the lobule of the lung; certainly they were not as distinct as the lobular patches present in human lobar pneumonia, nor could the intralobular structure described by Bezzola[21] and Ribbert[151] be definitely made out. The lung of the rabbit doubtless offers certain differences in the anatomical structure or arrangement of its lobules which may possibly explain these slight discrepancies. Furthermore, the posture of the animal doubtless influences the absorption and accumulation of exudates in the lung and thus, to some extent, the character of the lesion.

The Development of Experimental Pneumonia. It is obvious that the development of localized disease processes in the lung, as elsewhere, is determined by conditions referable either to the infecting micro-organism or to the animal infected. The infecting micro-organisms are extremely susceptible to environmental influences and thus exhibit considerable biological variation of both species and race. The biological character of the bacterial species as regards the peculiarities of growth and the elaboration of toxins and the special adaptation of the individual or race to the animal infected, commonly though inadequately expressed by the term virulence, are thus essential determining, but extremely variable factors in the development of all infections. On the other hand, the animals infected, within certain variable limits, afford favorable or unfavorable environments for the incitants of infection; in short, the animals are in varying degrees susceptible of infection.† This

* In distended or inflated lungs an artefact is often produced which should not be confused with these appearances.

† An important and co-operating factor intimately associated with the susceptibility of the animal is the chemotaxis. In animals very susceptible to certain infections it has been shown experimentally that, with extremely virulent cultures of the incitants, the chemotaxis is negative. In less susceptible animals or in immunized animals or with less virulent incitants the chemotaxis is in varying degrees positive.

susceptibility may be local as affecting certain tissues or parts of the animal or it may be systemic. When the bacterial incitant is extremely virulent or the animal very susceptible a systemic infection is induced, but when the bacterial incitant is less virulent or the animal only partially susceptible, a local infection is induced.

The morphological character of the disease processes depends in part upon the grades of susceptibility in the animal tissues, but chiefly upon the nature and virulence of the bacterial incitants, which, as noted above, are extremely variable. Different races of the same bacterial species thus often give rise to very different types of lesion in different or even in the same species of animal. Similarly, according to the degree of specialization necessary in the bacterial incitant, the different types of lesion may each be induced by a large or a small number of bacterial species or even by only one species, as in the so-called specific lesions. For example, in the lung, many different kinds of bacteria give rise to bronchopneumonia, but few to diffuse lobar pneumonia, and only one, the tubercle bacillus, to a specific productive necrotic process called tuberculosis.

Owing to the special anatomical arrangement of the epithelial, vascular, and lymphatic tissues of the lung, and to the physiological or pathological adaptation of these tissues, the lung surface acts, to some extent, similarly to the skin and mucous membrane as a barrier to infection, yet is peculiarly fitted not only for the rapid absorption and elimination of toxic material, but for the rapid diffusion of such material and the accumulation of exudates. The problem of infection in the lung is thus obviously complicated, and the relationship between the above-cited essential factors of infection more subtle than in other parts of the body. For most bacteria the normal lung is unfavorable, and similarly for the bacteria commonly found in pneumonic lesions the lung, as compared with other tissues, is, in most animals, a less favorable environment; thus for infection of the lung special adaptation or virulence of the bacterial excitant is essential. If this virulence be too great, the micro-organisms gain early access to and develop more rapidly in the other more favorable tissues of the susceptible animals. If this virulence be moderate, localized processes are incited in the lung, the surface of which, acting as a barrier to infection, prevents the invasion of the more susceptible tissues until the animal becomes, in a measure, immunized or the organisms acquire the requisite virulence for systemic infection. For the development of extensive diffuse lesions of the lung a relatively extreme adaptation or virulence of the incitant is obviously essential; thus these lesions rarely develop in animals very susceptible to the infection. Furthermore, bacteriæmias, whether temporary or terminal, are apt to complicate such disease processes. A relative systemic insusceptibility, whether natural to the animal

species or acquired by the individual,* is, therefore, an extremely important factor in the development of lobar pneumonia. For the formation of circumscribed or patchy lesions of the lungs less specialization or virulence of the incitant is required; thus the protective mechanism of the lung is usually an efficient barrier shielding the more susceptible tissues from infection, and bacteriæmias are comparatively rare. Occasionally, however, as in susceptible animals infected with incitants which possess or quickly attain a high virulence, a systemic infection supersedes the localized pneumonic lesion. Plague pneumonia is an apt illustration of the development of bronchopneumonia under these conditions, which, except for the lack of systemic insusceptibility, are the same as give rise to lobar pneumonia. Thus it is that in bronchopneumonia and in lobar pneumonia similar etiological conditions in slightly varying relationship give rise to slightly varying lesions differing only in type.

THE PNEUMONIC PROCESS IN MAN IN THE LIGHT OF THESE EXPERIMENTAL RESEARCHES ON ANIMALS. All grades of reaction from the idiopathic lung congestions (Maladie de Woillez) to the diffuse lobar pneumonic lesions may be induced by pneumococci in the lung of man. In these the different races of pneumococci exhibit wide variations in virulence. Carrière[82] found attenuated pneumococci in the lung congestions, whereas it is well known that those isolated from lobar lesions are usually extremely virulent. Eyre and Washbourn[61] tested four stocks of pneumococci: one from the sputum of a healthy person, three from pneumonia cases. The pneumonia cultures became excessively virulent by passing them through from eight to eleven rabbits, 0.00001 loop proving fatal in rabbits. The sputum culture was passed through forty-three rabbits before 0.001 loop was fatal, and fifty-three before 0.00001 loop proved fatal. The subsequent observations of these authors confirm the above-noted results.

It is well known that, relative to other species, man is more resistant† to pneumococcus infection. However, the resistance offered by different races of men varies greatly. Billings,[22] from the census report, found that the negro is markedly susceptible to pneumonic infection. Marchoux[118] reports an epidemic of pneumococcus infection of a bacteriæmic type occurring in a body of French colonial negro troops. Although disseminated lesions were present, well-

* This systemic insusceptibility may be acquired by individuals normally susceptible, in the early stages of the infection which may for a time be confined to the air spaces where the exudates collect; thus lobar pneumonia is occasionally induced in very susceptible animals. Such a fine balance of conditions is for the present at least beyond experimental control.

† The presence of the pneumococcus in the sputum of health and in many of the disease processes of the nose, throat, and ear suggests that more or less specific resistance may be developed at times in some if not in many individuals. By means of a special technique I have obtained agglutinin and precipitin reactions with the blood serum from certain animal species not usually susceptible to pneumococcus infection, and with the normal human sera tests these reactions were more marked and developed in higher dilutions. (Journal of Medical Research, 1903, No. 2, vol. x.)

developed pneumonias were comparatively rare. Kolle[104] noted a similar epidemic among the negroes of South Africa, but lesions were found in the lungs of some of these cases. Brodie, Rogers, and Hamilton[27] studied two epidemics of severe general pneumococcus infection, characterized by rhinitis and gastrointestinal disturbances, occurring in the Kaffirs. Pneumonic lesions were rare. Tostivant and Remlinger[182] describe the marked susceptibility of certain Arab tribes to pneumococcus infection and the difference in the lesions induced.

Aside from racial susceptibility, the individual at different ages and under different conditions offers striking analogies, in some instances to the susceptible, in others to the resistant, animal. In general, the newborn and the infant are remarkably susceptible to infection. At this age lobar pneumonias are rare; infection of the lungs with pathogenic bacteria gives rise to the bronchopneumonic type of lesion. Here, then, is a direct analogy to the susceptible animal. In the adult, as in the resistant or immunized animal, lobar lesions are more commonly found in the primary pneumonias; but, on the other hand, the adult may be rendered in varying degrees susceptible by other disease processes, and exudative pneumonitis developing under these conditions, the so-called secondary pneumonia, is more apt to be of the bronchopneumonic type.

It has long been recognized clinically that in the lobar pneumonias of man there is no definite relation between the extent of the lesion and the gravity of the infection upon which a prognosis may be safely based. This is even more pronounced in the experimental pneumonias in animals, and, as shown by the researches on animals, is due to the fact that extensive lesions may be incited by virulent infections when confined to the lung without seriously endangering the life of the individual; whereas less extensive lesions are often followed by general infections which terminate fatally. Thus the lesions in the fatal lobar pneumonias of old people are often small, sometimes unrecognized; whereas the lungs of a robust individual with good protective resources may be extensively involved, and yet recovery take place. As suggested by the researches on animals, the generalization of the infection is the real danger. Upon the determination of this only can a prognosis be safely based.

It is therefore evident that the various phenomena of pneumococcus infection observed in animal inoculation also occur in man. The rule of one is, however, the exception of the other; thus, general infections, except as transitory or terminal conditions complicating the local processes are comparatively rare in man, but common in the ordinary laboratory animal.

Summary and Conclusions.

As a result of the numerous and varied researches of other observers it has been determined that the bronchi and lung under

normal conditions are practically free from micro-organisms; that the secretions of the upper respiratory tract in both health and disease often harbor the bacteria commonly found in pneumonia, namely, the pneumococcus, the streptococcus, the staphylococcus, and the pneumobacillus; that the incitants of pneumonia may be carried to the lung by the lymph channels, inducing an interstitial pleuropneumonitis; or by the bloodvessels, giving rise to secondary metastatic processes; or, as is usual, by the air-passages, inciting the various lesions of exudative pneumonitis, of which two main types, the bronchopneumonic and the diffuse lobar, are recognized; and, finally, that the bronchopneumonic lesions, whether arising in man or induced experimentally in animals, may be incited by a great variety of bacteria, most frequently by the pneumococcus or the streptococcus; whereas, comparatively few species of bacteria give rise to diffuse lesions in animals, and in man practically but one species, the pneumococcus, ever attains the necessary specialization for the incitement of lobar pneumonia.

In the researches of others patchy or circumscribed lesions comparable to the bronchopneumonia of man, have been induced experimentally with comparatively little difficulty. Previous attempts to induce diffuse lobar lesions in animals, though successful in a few exceptional instances, have failed to determine the exact conditions under which the lesion develops and offer no reliable method of securing typical pneumonic processes.

By means of accurately controlled series of experiments which allowed of precise comparison, it was possible in my researches to determine the effect of increasing or diminishing the virulence of the incitant, the pneumococcus, in systemically predisposed, in locally predisposed, and in both systemically and locally predisposed animals. These experiments show that the incitement of diffuse lesions in the normal rabbit is extremely uncertain, and only possible in the predisposed rabbit when both the general and local susceptibility are increased and when organisms of comparatively low virulence are used. Thus, and owing chiefly to the fact that the lung surface acts as a barrier to infection, the development of acute exudative pneumonitis offers an especially clear example of the nice balancing of the essential conditions determining infection. These conditions are, on the one hand, the specialization or virulence of the incitant, and, on the other hand, the animal susceptibility, both local and systemic. Organisms of low virulence induce evanescent bronchial reactions; more virulent organisms by a local infection, give rise to the more typical bronchopneumonic lesions; while organisms of still greater virulence, if confined to the lung, incite diffuse processes of the lobar type, but if not so confined and bacteriæmic infection occurs, the lung lesions are less marked and of the bronchopneumonic type. The extremely fine balance of these conditions essential to the formation of lobar lesions in normal as

well as in predisposed animals is as yet for practical purposes beyond experimental control.

Finally, as a result of these systematic researches on normal and predisposed animals, an entirely new procedure was adopted: the preliminary immunization of the rabbits, so that extremely virulent cultures of pneumococci can be used without giving rise to bacteriæmic infection. The experiments with this procedure showed that diffuse exudative lesions comparable to the lobar pneumonia of man may be incited experimentally in the immunized rabbit; and that in securing this result there are but two chief variable factors, the virulence of the incitant and the immunization of the animal; both easily and accurately controlled by the routine technique of the modern laboratory.

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HEREDITARY ŒDEMA.

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Although the influence of heredity as a factor in the production of certain forms of œdema, not of cardiac or renal origin, was mentioned by Quincke in 1882, it was not until 1888, when Osler published the details of a case, that the subject attracted general notice in this country. This was probably due, first, to the eminent

position held by the latter writer in the medical world, and, second, to the exceptionally favorable circumstances that enabled him to obtain a full and accurate history of the patient's antecedents. Too often, in our attempt to learn the family history of any given case, are we met by absolute ignorance on our patient's part of facts concerning even his immediate progenitors, or receive information possessing the authenticity of tradition.

Rarely are we permitted to look back, with reasonably accurate vision, four, five, or even six generations into our patient's past. Cases have, however, been reported of the affection we are considering in which we are afforded such privilege.

Dinkelacker,[1] a pupil of Quincke, wrote a dissertation in 1882 on acute œdema, using as the basis of the essay cases referred to later by Quincke.[2] Among these was a case of a watchmaker, who had for years been afflicted with periodical attacks of acute œdema, whose son, a child of one year, had suffered from his third month with the same affection.

In 1885 Valentin,[3] who had occasion to see this family after the appearance of the papers of these two observers, adds the interesting information that another son, then two years old, not born when the above observations were made, was also afflicted with similar attacks from the first week of life. Another child, a daughter, had shown no sign of the affection up to the time of observation.

In 1885 Strübing[4] reports a case in a man, aged seventy years, who for forty-five years had had attacks of acute œdema of the face, throat, pharynx, and larynx, the latter so severe that extreme dyspnœa ensued. This would last a few hours and then subside. Between his sixty-third and sixty-eighth year he was entirely free from the throat attacks; then without any evident cause he felt pain on swallowing, with beginning inspiratory dyspnœa. This increased rapidly until in fifteen minutes it had attained such a degree that tracheotomy seemed unavoidable. Respiration was attended with the highest degree of orthopnœa, with action of all the accessory muscles. This condition lasted for a few minutes, then gradually subsided, until six hours later no sign of the distress remained. Now, however, œdema of the face and genitals developed. Four days later all disturbance had disappeared. More frequently than the attacks of œdema have occurred since his twenty-sixth year, at intervals of four to six weeks, attacks of severe vomiting, preceded by a slight sensation of abdominal pain, increasing in intensity up to the culmination in the vomiting. These attacks were attended by marked prostration and followed by sleep, out of which he awoke feeling well. At times the attack was ended in three or four hours, after vomiting four or five times. On other occasions it lasted twenty-four hours, with twenty to thirty repetitions of the emesis.

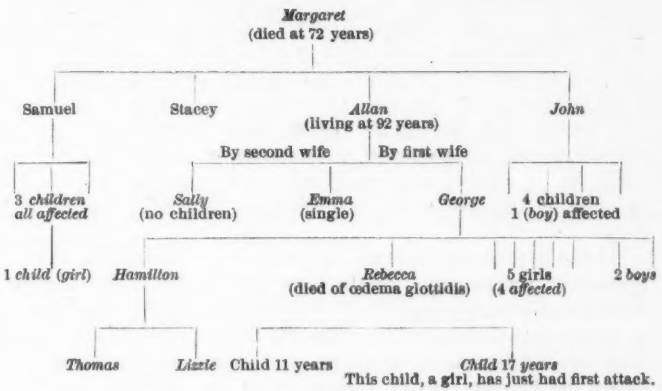
His sixteen-year-old son suffered from his third year with similar attacks, except that œdema was not so marked a feature. Much

more frequent were the attacks of vomiting, in which a large quantity of fluid was ejected. A daughter also suffered from attacks similar to those of her father.

Falcone[5] reports a case of acute recurrent œdema in a child, aged seven years, whose grandfather was afflicted with similar attacks.

Osler,[6] in 1888, reported a case of great interest in which, through the fortuitous recollections of some of the members of the family, and especially the unimpaired memory of a great-grandfather, aged ninety-two years, who had himself been afflicted for seventy-four years, a history of the affection extending through five generations, and involving twenty-two members, was obtained.

The characteristics of the affection in this family noted by Osler were: the occurrence of local swellings in various parts of the body; the almost invariable association of gastrointestinal disturbance, —colic, nausea, vomiting, and sometimes diarrhœa; the strongly marked hereditary disposition:



Krieger[7] cites a case in a man, aged twenty-five years, whose mother was also affected.

In one of Smith's[8] cases, that of a young woman, subject to recurrent attacks of œdema, the mother was similarly affected.

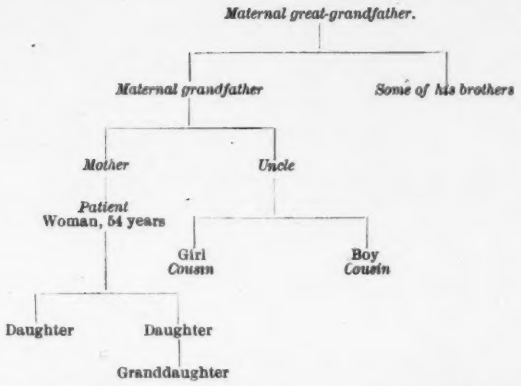
Fritz[9] gives the history of a man, aged twenty-three years, who fell and struck on the right temple. Shortly after the left eyelid began to swell, until the eye became completely closed. The swelling extended to cheek, lip, and neck. On entrance to the hospital there were cyanosis, dyspnœa, almost entire aphonia, and frothy expectoration. Examination showed the uvula swollen, the left tonsil, the left pillar of fauces, and the left side of the glottis very œdematous. During the night the swelling appeared in the right side of the face, subsiding in the places where it had first made its appearance. On the following day it entirely left the face, but appeared in the

right foot and ankle. Lungs and heart normal. Urine 900 c.c., 1022, acid. Urea, 28.8 grams. No albumin or sugar. He was otherwise well and had always been so, except that after drinking on an empty stomach, overeating, or after slight injuries, swelling, usually in extremities and eyelids, would ensue. These attacks had occurred since he was four years old. His paternal grandmother died of œdema of the glottis. One aunt had recurrent attacks of œdema. Two cousins, children of this aunt, died of œdema of the glottis. One of his sisters is also affected with attacks of glottic œdema. Both of his brothers died with the same form of œdema. Eight members in all were affected in this family.

Roy[10] mentions cases of acute circumscribed œdema in a mother and her daughter.

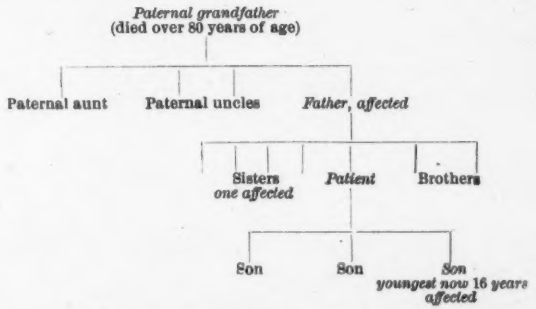
Ricochon[11] reports three generations of acute œdema, accompanied by colic, vomiting, meteorism, fever, and malaise. His cases show a close symptomatic resemblance to the cases of Strübing, already mentioned, and to those of Yarian,[12] which follow. This patient was a woman, aged fifty-four years, who since childhood had acute attacks, commencing with general malaise, followed by swelling of some part of the body, usually the face or extremities, sometimes the shoulders or chest. One or two days later she is taken with very severe sharp pain in the region of the epigastrium, occasionally elsewhere over the abdomen, with marked prostration. This is soon followed by nausea and vomiting, with severe retching. Mental emotion is capable of precipitating an attack with great suddenness.

At times with the œdema, or just as it is subsiding, there have appeared "purple rings" on the chest, neck, arms, and hypogastrium. After free vomiting the pain and œdema disappear, and such an attack in the forenoon does not incapacitate her for work in the afternoon. The attacks appear on an average of every two weeks, nine weeks being the longest period during which she has been free from its occurrence. Her mother had identical attacks from childhood, and died at the age of sixty-three years, "from dropsy." After the menopause she also had attacks of purpura. Her uncle on her mother's side had similar attacks, and died at the age of forty-two years, from œdema of the glottis. This uncle left a child, a girl, who suffers from periodical œdema without the gastralgia and vomiting. A brother of this child, now dead, also had attacks. Her maternal grandfather and some of his brothers had similar attacks, but without the pain and vomiting. Her maternal great-grandfather also suffered with the affliction, but he, too, never had the pain or vomiting. This is as far back as the affection can be traced. Her two children, both girls, while of irritable disposition, never showed signs of her trouble. One died of tuberculosis when twenty-one years of age. The other is living at twenty-five years of age and married. Her grandchild by this daughter has thus far shown no evidence of the affection.



Schlesinger[13] cites an instance in which the affection appeared in four generations. The patient, a man, aged forty-four years, has been subject for twenty-two years to the following attacks:

Commencing with a subjective feeling of irritation or depression, an exanthem appears on some part of the body. After six or eight hours this disappears, then on some portion of the body a rapidly developing swelling occurs, usually attended by pain in the epigastrium. This swelling develops with great rapidity, reaching its maximum in a few moments, lasts from one to three days, and then disappears. In the earlier years it occurred every half-year, later on at intervals of every ten or eleven days.



T. Wardrop Griffith,[14] of Leeds, reports a case of an adult woman, aged twenty-three years, who from infancy had been subject to attacks of localized œdema involving the hands, feet, shoulders, genitals, and throat. At the age of twenty-three years death occurred suddenly from laryngeal obstruction. Her father had been subject to similar attacks from earliest infancy. At the age of twenty-one years he had a laryngeal attack; a few years later another; and at the age of twenty-nine years a third attack caused his death. Examina-

tion of the larynx of the woman showed, in cross-sections, that the œdema involved not merely the mucous membrane, but also the deeper connective tissue, and even the substance of the muscles themselves, which condition Griffith thinks would prevent the abductors from enlarging the aperture during inspiration, and so lead to death.

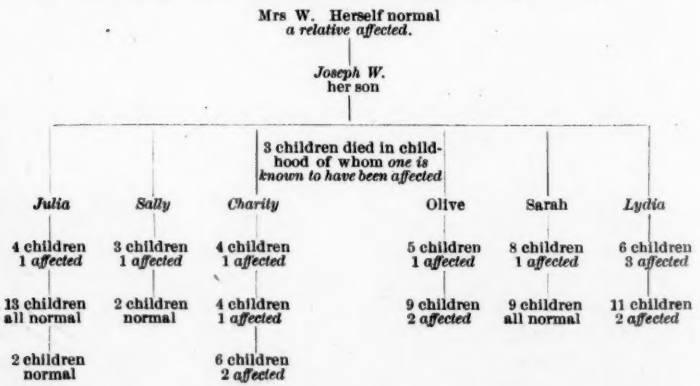
These instances leave no doubt of the influence of heredity in some of these cases of acute œdema. The characteristics of this affection are recurrent attacks of acute œdema in varying portions of the body, usually of rapid development and brief duration, and often associated with disturbances of the gastrointestinal tract.

We now come to the consideration of a form of œdema with quite different characteristics. This variety is as slow in its development and as sluggish in its course as the form we have just described is acute and transient.

Higier[15] says, in speaking of œdema not of organic origin, but occurring in connection with some neurotic condition: "It may appear and disappear in some hours or some days, but it may also last the life long. It is not rarely hereditary." This would seem to indicate that this author regards these two forms as in close relationship. It is questionable, however, whether we are justified in so considering them, on the basis of their clinical characteristics.

Heredity is as strongly indicated in some of these chronic cases as in the above-cited acute forms. The features peculiar to this chronic form of œdema are swelling in one or more extremities or parts of an extremity, of gradual onset, and usually life-long course, unattended by pain or disturbance of the general health. Some slight exceptions to this definition may be found in individual cases; such as transient pain, or the presence of some coincident affection, usually of the nervous system; but they are so seldom as to but emphasize the rule.

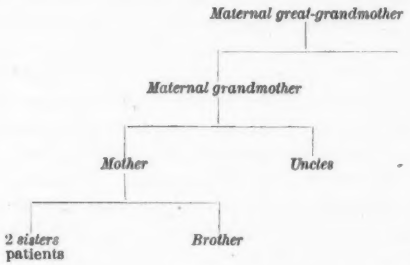
The following remarkable cases are reported by Milroy:[16]



Of six generations, comprising ninety-seven individuals, over 22 per cent. were affected. In the third generation there were nine individuals, all children of one father. Of these, three died in childhood of unknown cause. Of the remaining six, four lived to be over seventy years of age, and two were eighty and eighty-two years, respectively, at time of death. The other two died at the ages of sixty-six and thirty-eight years. This indicates in a striking way how absolutely harmless this form of œdema appears to be. We shall see that it is, in this respect, in sharp contrast to the form we have previously considered.

Jopson[17] reports two cases of marked subcutaneous œdema of the lower extremities of congenital origin in children, aged four years and one and one-half years, respectively, whose father, during his childhood, had a similar condition, which disappeared as he became older. The swelling in both cases pitted on pressure. In the older child the foreskin at birth was also involved.

In 1899 Meige[18] reported cases of a similar affection occurring in eight members of one family through four generations. The reader is referred to his excellent article for photographs of the condition.



In each of these cases the swelling came on at the period of puberty or slightly later, that is, from the thirteenth to the twenty-third year, and continued a chronic course, involving in some cases only one leg, in others both legs, in others both leg and thigh.

Desnos,[19] in speaking of chronic œdema, mentions that it may be hereditary, and thinks that when it is so it is usually down the maternal line. These cases of Meige, published eight years after this statement was made, seem to confirm the opinion. So few have been the cases reported, however, of this chronic hereditary œdema that it is impossible to determine that such is the case. It certainly is not so in acute œdema of hereditary nature.

In the cases reported by Dinkelacker, Quincke, and Valentin, and in the instances cited by Strübing, it was transmitted from a father to a son.

In Osler's cases this repeatedly occurs. In one instance the disposition can be traced through the male line for four generations;

great-grandfather, grandfather, father, and son each being subject to the attacks. This is strikingly exemplified in Schlesinger's cases, where also four generations in the paternal succession were affected. In Yarian's patient the maternal element is somewhat more evident, but even here we see that among her ancestors and relatives a father transmitted the disposition to several of his sons, and through one of these, not alone to a granddaughter, but to a grandson and great-grandson.

There have been many endeavors to solve the problem of the production of œdema. One of the earliest attempts at the solution of the question was that of Lower,[20] in 1669. Lower ligatured the inferior cava and claimed to have thereby obtained œdema of the lower extremities and ascites, as the result of the venous stasis, the blood serum passing through the vessel walls as through a filter. This was the mechanical filtration theory. Wherein the error in his experiment lay does not now appear. At all events, this was the prevailing view for two hundred years up to 1869.

Virchow,[21] in his *Handbook of Special Pathology and Therapy*, published in 1854, says: "I have never been able to convince myself that in mechanical dropsy the fluid passes through the walls of the veins. The location of the transudation is mainly the capillaries. With a certain degree of lateral pressure the capillary wall may be permeable for watery fluid."

This is a practical acceptance of the mechanical filtration theory for certain forms of œdema, but he says further: "Exceedingly difficult is finally the question of the primary essential or idiopathic, and the secondary, consecutive, or symptomatic dropsies. One may assume that these primary and essential dropsies are brought about by an arterial fluxion in parts whose blood and lymph vessels are in a state of disturbed nutrition."

In 1869 Ranvier[22] took up Lower's experiments and utterly failed to obtain œdema in that way. All the signs of venous stasis appeared, but œdema was not one of them. When, however, he cut the sciatic nerve on one side, on that side he obtained œdema, while on the other side no transudation from the vessels occurred. To the writer the most interesting result of Ranvier's experiments is the following: Œdema was only obtained when the sciatic nerve itself, outside of the spinal canal, was cut. When its roots of origin inside the canal before the accession of many sympathetic fibres were severed no dropsy resulted.

In 1877 Cohnheim and Lichtheim[23] published the results of numerous experiments. They concluded that a hydræmic condition of the blood in itself alone cannot cause œdema. For its production there must exist coincidently some injury to the vessel walls. They show that transfusion of salt solution, even to the extent of 64 per cent. of a dog's weight, is not followed by œdema of the skin. Such injury to the vessel walls may, however, be brought about in time by a

hydræmic condition itself. "The normal function of the vessel walls is dependent upon the continuation of normal circulation in the vessels. . . . It is hardly to be doubted that not alone the oxygen, but other constituents of the blood are equally important factors for the maintenance of the normal function of the vessels."

Sotnischewsky[24] thought that œdema could be produced by simple constriction of the veins, provided the total venous outflow of the limb was cut off, while every opportunity for the afflux of blood to the part was afforded. He found, however, that when he also cut the nerve supplying a vein, œdema occurred, even if the total venous outflow was not restricted.

Cohnheim[25] again, in 1882, emphasizes the greater facility with which œdema occurs in hydræmia from the poorly nourished and permeable vessels. He cites the experiment of Ostroumoff, in the course of his remarks. Ostroumoff irritated the peripheral end of cut lingual nerve with an induced current of gradually increasing intensity. He obtained a primary hyperæmia, followed in ten minutes by œdema, which, ten minutes later, had reached marked proportions. In 1884 some exceedingly interesting experiments were carried out by Landerer[26] to determine the part played by the elastic tissue in transudation. He found tissues subject to dropsy markedly deficient in elasticity, and concluded that this factor was one of great influence on the circulation of the blood and lymph. He considers œdema and inflammation also, an impairment of "the elastic equilibrium of the circulating fluids of the body." This subject was mentioned by Monro previous to 1777, for in the German translation of his work on dropsy of that date, on page 11, is the following: "Es giebt viele und mancherlei Ursachen von der Wassersucht. Die vornehmsten davon sind folgende. . . . Eine Erschlappung und Schwäche der Fasern. Diese Ursache fällt öfters vor."[27]

Gaertner,[28] repeating the experiments of Cohnheim and Lichtheim, thought that their injection of the salt solution was too rapid, and that œdema ensued when the fluid was more slowly introduced.

Gergens[29] found that in frogs the vessels allowed much more fluid to pass through when the medulla was destroyed.

Of much interest are the experiments of Salvioli.[30] He found that an excess of artificial hydræmia did not cause transudation into the subcutaneous tissue, but did to a certain extent produce œdema of some of the internal organs. When, however, he ligatured the renal and inferior mesenteric vessels, fluid did collect in the subdermal spaces of the abdomen, thorax, and thighs. From this he concluded that some vessels are naturally more permeable than others, and that when these vessels are cut off from the circulation, in this state of artificial hydræmia, those next in order of permeability permit transudation to take place. He regards the different organs as possessing different degrees of permeability, and thinks that the location of

such transudation may be varied by suppressing the vessels that under usual conditions most readily allow filtration.

Jankowski[31] says that œdema from hydræmia in itself alone does not exist, but that in such condition where the vessel walls are injured even slight disturbances of circulation suffice to produce transudation.

Recklinghausen[32] considered œdema the product of increased filtration of blood plasma, dependent on abnormal pressure in blood- and lymph-vessels or on chemical change in the blood plasma.

Heidenhain[33] and, at about the same time, Hamburger,[34] of Utrecht, advanced the theory that the capillary endothelium possesses powers of secretion, and is not merely a filtering agent.

Horsley and Boyce[35] saw the results of Ranvier's experiments confirmed in nine out of twelve cases, and, in an enumeration of the various factors in the production of œdema, quote the paper of Tigerstedt and Santesson[36] (which was not available to me) as disposing once and for all of physical theories, and of the dependence of transudation on mere variation in pressure on the two sides of a permeable membrane.

Hamburger,[37] in a paper on the regulation of the "osmotic tension" of fluids in the peritoneal and pericardial cavities, considers as factors in transudation, venous hyperæmia, increased permeability of vessel walls, and irritation of the capillary endothelium by some substance produced by disease, and later adds,[38] as a fourth factor, "retardation of absorption."

Lazarus-Barlow,[39] in a most valuable contribution to the subject, concludes that œdema is not caused by merely mechanical means, even in the cardiac variety; that there is no evidence of any damage to the bloodvessels, other than that caused by starvation of the same; and that anæmia, being in fact a starvation, in conjunction with non-removal of waste products, is an important cause of œdema.

The non-removal of waste products introduces the element of poisoning, which, he thinks, is a more important factor than mere anæmia.

Senator[40] believes that dropsy does not necessarily depend on disease of the kidneys, but upon a coincident injury to and consequent increased permeability of the blood- and lymph-vessels of the skin, and of the serous and mucous membranes.

Boddaert[41] says: "It is the general scientific opinion that obstruction of the lymphatics plays no part in the development of œdema by constriction," but concludes from his researches that œdema by constriction *is*, at first, at least, essentially lymphatic.

He considers, as a result of direct experiment, that the œdema produced in one extremity by ligature of the lymphatics alone is identical in kind with that produced in the other limb by constriction of its entire circumference (in the upper part of the thigh). His researches were conducted on rabbits.

Opitz[42] presented, in 1899, an excellent general consideration of the whole subject of œdema.

He thinks that the filtration theory received a hard blow from the experiments of Cohnheim and Lichtheim, whose work he considers the starting-point for the modern theory of œdema.

Howell[43] classes œdema as follows: Œdema of engorgement, œdema of inflammatory origin, that of hydræmic or cachectic nature, and that of angioneurotic character. Changes in the vessel walls of nutritive character, qualitative changes in the blood and toxæmias resulting in malnutrition and nerve irritation, are all causative factors. Instances of such blood conditions are seen in anæmia, chlorosis, scurvy, slow starvation, chronic discharges, etc., and all debilitating influences resulting in hydræmia.

Funck,[44] in an exceedingly interesting paper on the physiology and pathology of dropsy, says that it has been experimentally shown that, within moderate limits, as in ordinary disease, neither a diminution of albumin nor an excess of water in the blood is sufficient to cause œdema. To produce œdema, something more is required than more facility of filtration of watery blood, in fact, malnutrition of the vessel wall, lessened elasticity from vasomotor paralysis, rendering the vessels more permeable for fluid.

Albu[45] believes that a watery condition of the blood, with loss of albumin, favors the transudation of serum from the vessels; that a "hydræmic plethora," with lessened outflow of fluid, tends to the same condition; while the *sine qua non* is an increased permeability of the vessel walls. These three theories are practically those of Bright, Bartels, and Cohnheim, respectively, combined.

Among the latest works on the causation of œdema known to the writer, and which practically brings the subject up to date, is the interesting work of Jacques Loeb,[46] of Chicago. Loeb considers the filtration theory utterly erroneous. He says: "I consider that the power for the movement of fluid in the tissues in cases of œdema (as in all other cases) is essentially to be sought for in osmotic force, and that the œdematous conditions, that is to say, the penetration of fluids into the tissues, occur when the osmotic force in the tissues is higher than that of the blood and lymph. In other words, the œdema must have as its basis such causes as raise the osmotic force of the tissue or lessen the osmotic force of the blood and lymph." This may be a change in the tissues of chemical nature that increases its osmotic force. Loeb produced such a change in a muscle by totally shutting off its circulation, and suggests that it may have been due to lack of oxygen. He shows that the osmotic pressure may be 300 times the degree of intravascular pressure that has been thought sufficient to produce the highest degree of œdema of the lungs.

Many experiments with frogs showed that a given muscle in a limb, when the circulation to the limb was totally restricted, absorbed fluid to from 1 per cent. to 3 per cent. of its weight in eighteen hours,

15 per cent. in forty-eight hours, 25 per cent. to 40 per cent. in seven days. A similar result ensued when the muscle was removed and placed in salt solution.

This chemical change in the muscle, which increases its osmotic force, and is apparently due, he thinks, to lack of oxygen, is accompanied by acid formation. Osmotic force may be increased in the tissues by alkalies, acids, and loss of water.

"The occurrence of œdema is brought about by chemical changes in the tissues. These chemical changes influence first the osmotic force in the sense that in the tissues that are œdematous it is higher than in the blood and lymph. Second, these chemical changes may also bring about morphological changes."

As Sewall[47] pointed out some years ago, there can be no question but that osmosis in living animal tissue is a different problem than it is in dead membrane. The endothelial walls of the capillaries are composed of living cells engaged in active vital process, vital, at least, as regards their own existence, if in no other way. That this living cell membrane allows the fluid of the blood or tissues to pass through it, subject only to the law of diffusion, as applicable to dead inert membrane, seems to the writer extremely problematical, although, perhaps, possible. Another source of error is the assumption that deductions drawn from experiments on lower animals are, without further qualification, applicable to physiological or pathological processes in the human being.

Not alone do different animals vary greatly in the degree to which a physiological or pathological process may be carried out, but also corresponding organs in the different species may possess functions differing greatly in degree, if not in kind. This is, perhaps, nowhere more evident than in the cutaneous covering of the various animals. Thus the skin of man is an organ of excretion of the utmost importance, while in the dog this is, by comparison, a function of infinitely less value. In the rabbit and guinea-pig such is also the case, while in some animals scarcely any analogy exists. The dog, and occasionally the rabbit, have, as a rule, been the animals employed in the attempt to solve this question. It would seem that such marked variation in the function of an organ, in man of the greatest importance, in the animals experimented upon of relatively little importance, in the elimination or retention of the watery constituents of the body, must have its influence on the results of these experiments, and should be considered in the deductions drawn therefrom for application to similar processes in the human being.

However, the actual process of transudation may take place, we know, beyond all reasonable doubt, that the *exciting* factor in this process may be, in numerous cases, of neurotic nature. It is not necessary to go beyond the limits of the human species to find convincing evidence of this fact.

The occurrence of œdema in traumatic or surgical injury to a nerve or in other nerve disturbance has frequently been seen.

The œdema following nerve section; the transudation occurring in the area of distribution of a nerve which has been the seat of neuralgic pain; the œdema occasionally met with in neuritis; that of paralyses, and that sometimes seen in tetany are all instances in which the neurotic factor is apparently direct. Further evidence is found in the occasional occurrence of not only a circumscribed but a unilateral œdema, of which a case will be noted among these here reported. (Fritz.) These cases are somewhat analogous to those of unilateral hyperhidrosis or hemidiaphoresis sometimes seen. The occurrence, simultaneous with the transudation, of symptoms of undoubted nervous origin, or the occurrence of the same at other times, or occasionally in alternation with the œdema, furnishes also strong presumptive evidence of its neurotic character. The extremely rapid onset, development, and disappearance of the acute attacks can hardly be accounted for on any other than a neurotic basis.

Finally, the heredity itself in the cases above mentioned strongly suggests a neurosis.

Of interest in this connection are the cases of periodical vomiting described by Leyden,[48] who cites their analogy to the "gastric crises" of Charcot. These attacks closely resemble those of Strübing's and Yarian's cases, apart from the œdema. They were, as in the case of Strübing's younger patient, accompanied by the vomiting of large amounts of watery fluid. In none of these cases did œdema ever appear, but the gastric symptoms are practically identical with those seen so frequently in these cases of acute œdema.

The neurotic element in the chronic cases is not evident, although Meige is inclined to consider them analogous to the trophic disturbances seen in lesions of the cord.

No more curiously interesting affection exists than this recurrent acute œdema. Here we have in one family a man living in unimpaired vigor of mind and body at ninety-two years, having suffered with the affection for seventy-four years, while in his family a child died of the affliction in early life, and an adult woman forfeited her life to the same disease. That death may be narrowly escaped is illustrated by the fact that his mother at one time nearly died of "shortness of breath," but, nevertheless, lived to be seventy-two years old.

That death may come with great suddenness and without warning is shown by Griffith's case. This woman was playing on the floor with her baby, apparently in perfect health, when she was seen to suddenly put her hand to her throat as if she felt trouble there and immediately fell over dead.

This affection has occasionally been regarded as one of little seriousness to life. It is, however, a condition of serious import, and, once occurring, renders the patient's future always insecure.

Krieger's case was found dead in bed, and autopsy showed that death was due to œdema glottidis. Five of the eight members of the family cited by Fritz died of glottic œdema, including both of the patient's brothers.

Griffith's case died at twenty-three years and her father at twenty-nine years, both of œdema of the glottis.

These cases are only those occurring in the families where the affection manifested some hereditary tendency. Many fatal cases have been recorded in instances of acute recurrent œdema where heredity was not manifested, and which, therefore, are not included among those we are considering. But if we consider the mortality in these hereditary cases alone, we shall see that the affection shows a death rate of about 16 per cent.; while of the remaining cases, 6 per cent. had had attacks in which death was imminent.

This is a mortality in strong contrast to the prognosis given by some writers for acute recurrent œdema; and it will at once be evident why this is so, when we consider that cases of this affection are rarely under the observation of any one observer for any prolonged period of time.

The full life history of the individual is, therefore, not obtained.

In a somewhat extensive review of the general subject of acute œdema previous to the study of the hereditary cases, it was evident to the writer that the mortality was much greater than was generally considered, but no conception of as high rate as the above percentage indicates was obtained. It would seem, however, that we must be nearer the truth in deduction based on these hereditary instances, for here we know the life history of many of the individuals, and further knowledge of the ultimate fate of those still living would tend not to diminish but to rather increase the death rate.

In the fatal cases death was due, almost without exception, to œdema of the glottis.

If in the adult death may occur with the extreme suddenness seen in so many of these instances from obstructive œdema of the throat, it might well be thought that in the child this would be much more likely to occur.

Curiously enough, however, the majority of the deaths in the cases here reported occurred in adult life, notwithstanding the fact that many of the individuals had been afflicted with the affection in childhood.

Another singular fact is that while in almost every family there were many cases that began in childhood, there were a number in which the affection did not appear until after this period; and in one family, in four generations, no case occurred until adult life was attained.

Direct exciting cause seems often to be present in the individual attacks. In a number of instances trauma appeared responsible for the onset; in others exposure to extremes of temperature or emotional excitement were apparent factors. These can but be regarded as merely the sparks that induce the explosion of nerve force, already in a state of hereditary unstable equilibrium.

Of the ultimate neurotic nature of the affection, it would seem that there could be no serious doubt.

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REVIEWS.

A Treatise on Orthopedic Surgery. By Royal Whitman, M.D., Instructor in Orthopedic Surgery in the College of Physicians and Surgeons of Columbia University, New York; Associate Surgeon to the Hospital for Ruptured and Crippled; Orthopedic Surgeon to the Hospital of St. John's Guild; Chief of the Orthopedic Department of the Vanderbilt Clinic; Member of the Royal College of Surgeons of England; Member and some time President of the American Orthopedic Association; Corresponding Member of the British Orthopedic Society; Member of the New York Surgical Society, etc. Second edition, revised and enlarged. Illustrated with 507 engravings. Philadelphia and New York: Lea Brothers & Co., 1903.

The second edition of this book triply applauds its author. The first edition, profusely illustrated by line and half-tone prints, completely and concisely presented the best and latest thought of to-day in orthopedic surgery. The prompt exhaustion of this edition is but a merited acknowledgment of the appreciation of the medical bookbuyer. The bookmaker's tribute to the writer follows and will be welcomed by the booklover, since it accords a more generous, fitting, and attractive publication to the second edition. In the latter, contrasted with its predecessor, suitably selected paper has vastly improved the printing of the half-tones, while the judicious leading of a smaller printed page, framed with wider margins, and marked by a freer use of boldface headings, has much increased the ease of reading and reference and materially enhanced the beauty as well as the number of the new book's pages. Not resting on the double laurels won by the first edition, the author has proceeded to deserve a third variety on account of new features introduced in text and illustration in the second edition. Not only has the work been brought abreast of the moment by a number of valuable additions, but the matter of the first edition has been revised and in a couple of instances reclassified.

The Lorenz refinement of the Pravaz and Paci manipulative articulation by "bloodless method" of congenitally unarticulated hip-joints is described in minute detail, and step by step illustrated through each stage of operation, fixation, and after-treatment. This supplement to what in the first edition was rather a comprehensive

chapter will doubtless be scrutinized first and with ungrudging approval by each reader of the new volume. Congenitally malformed hips, however, are comparatively rare deformities, and the greater usefulness of this book lies in the excellent chapters, with which we are familiar, dealing with the more prevalent tubercular lesions of spine and hip, with rachitic deformities, with scoliosis, with paralyses, and the congenital and other distortions of the feet, including the practically universal ones due to conventional shoeing, and not forgetting the newly inserted method of correcting hallux valgus by Sampson's ingenious toe-post. One cannot glance at these chapters, in either edition, without admiration for their illustrative demonstration—clear beyond mistake—of the most modern orthopedic methods and apparatus.

The topical division of subjects with subclassifications on a pathological basis has been preserved, and doubtless will be of practical assistance in reference for physicians not devoted to this specialty. On the other hand, both scientifically and for the instruction of students, it would seem preferable to group the subjects according to their pathological origin and subdivide them in reference to their anatomical distribution. J. M. S.

RADIUM AND OTHER RADIOACTIVE SUBSTANCES: POLONIUM, ACTINIUM, AND THORIUM. With a consideration of Phosphorescent and Fluorescent Substances, the Properties and Applications of Selenium, and the Treatment of Disease by the Ultraviolet Light. By WILLIAM J. HAMMER, Consulting Electrical Engineer. New York: D. Van Nostrand Co., 1903.

COMING at this time, when the attention of students of both pure and applied science is focused on the extraordinary phenomena manifested by radium, polonium, and their allies, this little work is singularly opportune. Within the brief compass of 72 pages the author presents clearly and concisely a great deal of very interesting and instructive matter.

To the physician the subject has a double interest: he follows with appreciation the work of the physicists in their investigations into those activities, the manifestations of which have so changed our views of matter; he seeks for therapeutic possibilities in the practical application of this radioaction against disease.

The first part is devoted to a consideration of phosphorescent and fluorescent substances, which the author aptly likens to "step-down transformers," in that they lower the vibration frequency of ultraviolet rays to such a number that the human eye can appreciate them. The fact that many of these substances respond to the stimulation of radioaction and emit light makes their study one of

importance. As an example of this is given the fact that a diamond will phosphoresce from stimulation by radium, thus differentiating it from an imitation diamond.

Briefly and clearly the author gives the history of radioactive substances from their extraction from the common source, pitchblend, through the record of observed facts and ingenious hypotheses. The author discusses the substances in the order of their activity, taking uranium as a standard; the emanating rays are classified according to their power of penetration and susceptibility to deflection by a magnet, and, further, their properties are compared with those of x-rays. Several interesting radiographs are shown, giving the photographic record of the power of penetration of the emanations from the radioactive substances through materials of varying resistance. In conclusion, we are given a short though entertaining account of the Finsen Light Institution and the method of treatment employed there, some of the results in cases of lupus vulgaris being shown by photographic plates. H. M. W.

INFECTION AND IMMUNITY, WITH SPECIAL REFERENCE TO THE PREVENTION OF INFECTIOUS DISEASES. By GEORGE M. STERNBERG, M.D., LL.D., Surgeon-General, U. S. Army (retired). New York and London: Putnam & Sons.

To present the subjects of infection and immunity as these phenomena are now interpreted in a form which is intelligible to the non-medical reader is indeed a difficult problem. Owing to the new technical terms which the investigations upon antitoxins, agglutinins, precipitins, and bacteriolysins have brought into use, and to the complexity of Ehrlich's side-chain theory, these subjects have been practically omitted as being unsuitable for popular treatment. The volume therefore narrows down to discussions upon the general subjects of "susceptibility to infection," "disinfection," "immunity," and a series of chapters upon the various infectious diseases which form the second and major part of the volume. Bubonic plague, Asiatic cholera, typhoid fever, etc., are all discussed separately. Each disease is considered from an historical, etiological, and epidemiological standpoint, while special regard is paid to prophylaxis and measures of prevention. Technical terms are avoided as much as possible and the main facts regarding each form of infection are given in a concise, clear, and interesting manner. The chapters on yellow fever and malaria are particularly good.

Perhaps the title of the book is somewhat misleading, but the text is none the less interesting. W. T. L.

DIE FERMENTE UND IHRE WIRKUNGEN. VON CARL OPPENHEIMER, Dr. Phil. et Med.; Assistent am Thierphysiol. inst. d. Landwirth. Hochsch, Berlin, Zweite Neubearbeitete Auflage. Leipzig: F. C. W. Vogel, 1903.

THE general subject of Ferments has assumed so much importance within the last few years that without a proper knowledge of their action one is at a loss to explain many of the processes concerned in physiology or pathology. A book such as this is particularly acceptable, and it is really impossible to overestimate its value. The subject is treated in a purely scientific manner and each chapter contains such a wealth of information that it may be read many times without exhausting the benefits to be derived from it, so carefully has the material been collected and so concisely put forth. The first and minor portion of the book deals with the subject in general terms, while in the second portion the various ferments are grouped together in sections, but discussed fully in separate chapters. Cytolysins, agglutinins, and precipitins receive recognition and are classed as substances related in a way to the true ferments. The book has both subject and author indices. One realizes the great care and precision with which the book has been prepared when he finds over 1500 references to literature. The book numbers 439 pages in all. W. T. L.

SURGICAL DISEASES OF THE ABDOMEN, WITH SPECIAL REFERENCE TO DIAGNOSIS. By RICHARD DOUGLAS, M.D., Formerly Professor of Gynecology and Abdominal Surgery, Medical Department, Vanderbilt University, Nashville, Tenn.; ex-President of Southern Surgical and Gynecological Association, etc. Illustrated, 883 pp. Philadelphia: P. Blakiston's Son & Co., 1903.

SURGEONS both in their journal articles and text-books have, we feel, paid undue attention to operative technique to the neglect of the important question of diagnosis. It is therefore with pleasure that we review this book on *Surgical Diseases of the Abdomen*, which deals almost entirely with the diagnosis of these conditions and which is yet written by a practical surgeon. A book dealing with the diagnosis of abdominal diseases from the surgical point of view has been a want felt by all surgeons, and the present volume bids fair to supply that want very satisfactorily. Abdominal surgery has become a wide field and has extended its boundaries far into the territory formerly considered entirely the domain of the medical man. Consequently the question of diagnosis in this field of surgery is of as much, if not more, importance to the surgeon than to the physician.

The book before us presents each of the subjects under discussion in a most extensive and satisfactory manner. At the close of each chapter is a list of references which will be found of great value to the reader who desires to further investigate any particular subject. The illustrations are not profuse, but supply every want.

It is impossible in a review of this kind to comment upon each portion of the book, but nevertheless certain comments may not be out of place.

The first chapter is an excellent one on Peritonitis, in which the symptoms and diagnosis are presented in a most comprehensive manner. Instead of describing extensively the steps of the surgical treatment, the author briefly presents the surgical indications. Although we agree with him that drainage is too constantly employed in pelvic work, we are not prepared to say the same, as he does, of appendiceal work. He heartily approves the postural drainage, suggested by Fowler, which has proved so very satisfactory in cases of peritonitis. The diagnosis and surgical indications of typhoid perforation are carefully considered, but in our judgment the author does not urge with sufficient energy immediate operation as soon as symptoms indicate perforation. It is now practically agreed by all having experience in this condition that it is a mistake to delay operation for the recovery from shock, but that the sooner the abdomen is opened and properly treated the better will be the result.

We fully concur with Douglas in his attitude toward the exploring needle as a diagnostic measure in liver abscess. He states that the needle should not be employed unless the surgeon is prepared to operate at once in case pus is found.

The portions of the book dealing with diseases of the kidney and with abdominal injuries meet with our particular approval. The latter portion of the volume is devoted to surgery of the female pelvis, and is not proportionately as extensive as other parts. One criticism that might be offered is that the diseases of the ureter have not been considered.

This book is one which every surgeon and every physician can read with profit, and it will undoubtedly take its place as a most satisfactory book of reference. J. H. G.

CANCER AND PRECANCEROUS CHANGES, THEIR ORIGIN AND TREATMENT. By G. H. FINK, M.R.C.S., L.S.A. LOND., Major Indian Medical Service (retired). London: H. K. Lewis, 1903.

THIS pamphlet is a highly speculative and often vague discussion upon the changes in the animal organism as well as in the surrounding hygienic conditions which may lead to the development of

cancer. An analogy is drawn between the life-cycle of the malarial parasite and the life-history of cancer, while great importance is given to the hypothetical "materies morbi" of new-growths. Much of the dissertation is far from lucid, owing both to the abstruse nature of the problems dealt with and to the faulty English used. To some persons the book may prove interesting, but scarcely instructive. W. T. L.

A TEXT-BOOK OF OBSTETRICS. By J. CLARENCE WEBSTER, M.D., F.R.C.P.E., F.R.S.E. Philadelphia, New York, and London: W. B. Saunders & Co., 1903.

THIS is a thoroughly good work. Not only is the practical side of the subject well handled, but, in addition, the scientific receives its required consideration. Throughout the author has shown a nice sense of proportion, and seems to us to have succeeded in his endeavor to make a book suitable both for the needs of the active practitioner and the scientific student.

As might be expected, his section upon Placentation is especially good, as are the chapters on Ectopic Pregnancy and Eclampsia.

His chapter upon Pelvimetry is up to date in every way, even to the figuring of Ehrenfest's pelvigraph and kliseometer.

Throughout the volume his advice as regards treatment is marked with most satisfactory conservatism.

The consideration of the subject of "Puerperal Infection" is, in our opinion, one of the most valuable portions of the whole book. In this chapter the subject is considered in a thoroughly scientific manner, and the treatment is in accord with the views which receive the adherence of most experienced men.

In a word, the author has produced a very satisfactory volume which, undoubtedly, will receive the commendations of the profession. W. R. N.

A TEXT-BOOK OF OBSTETRICS. By BARTON COOKE HIRST, M.D. Philadelphia, New York, and London: W. B. Saunders & Co., 1903.

FOUR editions since first issued, in 1898, is a record which makes the formal review of this work a rather useless procedure.

To be a satisfactory subject for review a volume should have some rather glaring faults either of omission or commission, thus enabling the one who criticises to express his opinion without being compelled to make a very searching examination. Unfortunately, this

volume is not satisfactory from the reviewer's standpoint, as a rather intimate knowledge of the earlier editions and an examination of the changes and added material in the present one have not enabled us to find any points about which one can write adversely. We are, therefore, compelled to consider the good points of the book, a study which, while not as exciting to us, is, nevertheless, in the present instance, one which affords us decided satisfaction, as we believe this to be one of the best books on obstetrics published up to the present time for the use of both the undergraduate student and the man engaged in active practice.

As samples of the general excellence, we would refer to the chapters upon the Pathology of the Puerperium, the Pathology of the Newborn Infant, and the section devoted to the Major Obstetrical Operations. The chapter on Puerperal Sepsis is also particularly complete, and we are glad to note that while the use of the Döderlein or Menge tube is described and advocated as an aid to diagnosis, its limitations and the possible factors of inaccuracy in its use are clearly defined.

The book is even more profusely illustrated than the previous editions. W. R. N.

ROLE DES POISON DU BACILLE DE KOCH DANS LA MENINGITE TUBERCULEUSE ET LA TUBERCULOSE DES CENTRES NERVEUX. Par DR. P. F. ARMAND-DELILLE. Paris: G. Steinheil, editeur.

THIS monograph is a study upon the effect which different poisons isolated from the tubercle bacillus may produce upon the central nervous system. The research is divided into three parts. The first part deals with the experimental aspect of the subject; the second with the histological lesions, and the third gives the conclusions which the author draws from his work and the theories which may be deduced therefrom. From the experimental investigations it was found that the tubercle bacillus is capable of producing two varieties of poisons which act in different ways upon the meninges and brain. One group has a local action. It causes more especially caseation of the tissue, and through the mechanical action of these lesions vascular alterations follow in the surrounding tissue, resulting in degenerative changes of the nervous elements. The second group of poisons is of a diffusible nature and gives rise to phenomena of nerve-cell intoxication without evident histological modifications in either the nerve cells or meninges.

Tuberculosis of the meninges, studied from the histological standpoint, was never complicated by actual inflammatory lesions of the elements of the nervous tissue; but important degenerative alterations were found in the nervous centres immediately surrounding

the diseased meninges and were ascribed to the changes in the blood-vessels.

The author, from these observations, formulates a conception of the pathological physiology of tuberculous meningitis. Three periods may be distinguished in the genesis of clinical symptoms. The first period, the stage of excitation, is explained by the circulatory disturbances in the cortex, and in a small measure by the toxic phenomena; the second period is characterized by symptoms of paralysis of the cortex, which seem to be produced by the toxic phenomena, and the third period ends in death, caused by paralysis of the spinal cord and medulla from intoxication by the diffusible poisons of the tubercle bacillus. W. T. L.

A SYSTEM OF PHYSIOLOGIC THERAPEUTICS. Edited by SOLOMON SOLIS COHEN, A.M., M.D., Senior Assistant Professor of Clinical Medicine in Jefferson Medical College, etc. Philadelphia: P. Blakiston's Son & Co., 1903.

VOLUME VIII. REST, MENTAL THERAPEUTICS, AND SUGGESTION. By FRANCIS X. DERCUM, M.D., PH.D., Professor of Nervous and Mental Diseases in the Jefferson Medical College of Philadelphia, etc. Pp. 318.

VOLUME X. PNEUMOTHERAPY, INCLUDING AEROTHERAPY AND INHALATION METHODS AND THERAPY. By DR. PAUL LOUIS TISSIER, one time Interne of the Paris Hospitals; Assistant Consulting Physician to Laennec and Lariboisière Hospitals, etc. Pp. 479.

VOLUME VIII. presents much that has been the subject of other volumes in times gone past and also much that is of more recent date. If the author had merely given us a modern presentation of "Rest and Pain," as Hilton taught us, we would have been only grateful for the opportunity of again reviewing a book which made a deep impression upon us in our earlier career. But he has done more, for he has traced the connection farther than our fathers and added to it the best of Mitchell and of those who have introduced modifications of more or less importance. In pointing out how far this is applicable to the treatment of hysteria and the symptom-complex of neurasthenia we find the field enlarged, and conditions more or less allied to the latter subjects offered for discussion. Hypochondria, according to the author, becomes a "readily differentiated clinical entity," and with this view we will agree so far as concerns the plan upon which he bases his hopes for relieving those troublesome patients of their symptoms. At any rate he makes them a class by themselves, and in that differentiation we are more

hopeful both for the neurasthenics and hysterics. In the sixth chapter, on the application of rest in chorea and other functional nervous diseases and in organic nervous diseases, we find a curious assemblage of symptoms and diseases, although we are not disposed to be critical, for the practical points abound and the large experience of the author is well in evidence. The therapeutics of mental diseases is well presented in two chapters comprising eighty pages. To those who believe that the subject cannot be summed up in mechanical and chemical restraint we commend this section of the work. So thorough has the writer been that we are of the opinion that those whose especial work lies in the treatment of these unfortunates will find much to learn, while those in the broader field can find much that the physician should know and apply in the way of prevention. Finally we come to suggestion for which, as is pointed out, there is a legitimate field and, as we all know, one that should be understood only to condemn. For those who have gone over the dreary wastes of speculation or read pages of invective these chapters are refreshing.

In Vol. X. we have a book of a different type—an effort to assemble together practically all that can be said in favor of the method, and in this compilation an *ex parte* argument is presented with the resultant lack of perspective. Granted that this method has been neglected, its presentation need not include the antiquated and the obsolete, which obscure the present. Completeness may suggest that all be presented, but in every-day and practical work they are unnecessary. Air as a therapeutic agent is presented from all viewpoints—composition, density, temperature. The therapeutic applications follow closely upon the physical and chemical facts. The special therapeutic indications are not the subject of separate chapters, but are included in the broader statements, but, however, with sufficient differentiation of particular interest, as in the chapter on "General and Respiratory Gymnastics and Mechanical Pressure Methods," which, however, should be read in connection with Vol. VII. of this series. In the second part "Inhalation Methods and Therapy" will doubtless prove to be of greater interest to the physician. Dealing with gases, fumes, and vapors in general, the author takes up the medicaments suitable for use (vapors, atomization of liquids, insufflation of powders) in satisfactory detail. If any matter of importance has been omitted we have failed to note its absence. In this portion the literature is full, the directions precise, and the indications fully set forth. How much can be accomplished by these methods only one who has intelligently practised them can believe. As one lays down this volume he must admit that it contains a mass of information of real value; that it has reconciled many hitherto disputed points; that theory has been modified to the point of furnishing a working basis for practice, and that all methods and matters are readily accessible. If, as in other volumes of the

series pharmacology is in evidence to a greater extent than the plan of the work would seem to indicate, we must remember that no complete scheme of therapeutics can be built on any one or on all physical agencies combined, and that physiological properties are possessed by matters other than those presumably here presented. Excluding what has seemed to us as unnecessary in a book which is to appeal to the practising physician, we believe that this volume represents the present state of our knowledge upon this subject, and that its information is in a presentable form, for which the reviewer and reader will congratulate Drs. Eshner, Brickner, and Goepp for their skilful and painstaking translation. R. W. W.

A THESAURUS OF MEDICAL WORDS AND PHRASES. By WILFRED M. BARTON, M.D., and WALTER A. WELLS, M.D. Philadelphia, New York, and London: W. B. Saunders & Co., 1903.

THE most striking feature of this work is its entire originality both of conception and execution. There is no other book just like it, and it has been so carefully compiled and covers the ground so thoroughly that we doubt if there will be room for a similar publication for years to come. The method of its use is explained in a well-written introduction. It is intended to play for medical literature the part which Roget's *Thesaurus of English Words and Phrases* has long done for general literature. It is not a medical dictionary because it does not furnish definitions, but merely synonyms, and in fact reverses the ordinary dictionary method, as instead of supplying a meaning or idea for a given word, the Thesaurus supplies the word necessary to express the idea which we have in our mind. The persons to whom it will prove especially useful will undoubtedly be those who, while deficient in medical education, are employed at work in medical literature. Thus, as its authors claim, it will possess great value to stenographers engaged in transcribing the proceedings of medical societies or reporting medicolegal testimony. It will also be of great value to translators of medical works.

Although the authors suggest its value to lawyers, journalists, or novelists who are dealing with subjects requiring the employment of technical medical terms, nevertheless, we take leave to express the opinion that it would be most unfortunate should these three classes of laymen attempt to write technical descriptions from its pages. We could imagine the ridiculous effect produced in their writings by the choice of some of the synonyms which are given for words in ordinary use, and as there is no guide to the definition of the various synonyms, the *Thesaurus* would leave them at perfect

liberty to choose anything they might desire; and when it is remembered that medical men no longer talk the ridiculous jargon which amuses us so much from the lips of Dr. Slop in *Tristam Shandy*, we can but conclude that it is much safer for a layman not to provide himself with a *Thesaurus*, but to write in the ordinary vernacular. To all those engaged in medical literary work, this book will prove invaluable. Its thoroughness, accuracy, and the skilfulness with which the subject-matter has been arranged leaves nothing to be desired in it as a work of reference. F. R. P.

Die Krankheiten der oberen Luftwege. Aus der Praxis für die Praxis. Von Prof. Dr. Moritz Schmidt. Dritte sehr verbesserte Auflage. Berlin: Verlag von Julius Springer, 1903.

This valuable work of Prof. Schmidt, which has long been a standard text-book in Germany, deserves to be much more widely known and consulted in America than is the case. It is probably too advanced and thorough to be of much service to the ordinary American medical student as a college text-book, but as a work for consultation and reference, it should be in the library of every physician who is engaged in doing special work in diseases of the nose, throat, and ear. One is especially struck with the author's breadth of view in regard to the connection between disorders of the nose and throat, and constitutional diseases or conditions, which is manifest throughout the entire work. The author is thoroughly conversant with all of the most recent methods of diagnosis and treatment, and, what is probably more remarkable in a German, he is thoroughly familiar not only with Teutonic medical literature, but with the work being done by physicians belonging to other nationalities. It is to be hoped that a translation of this invaluable work will at some time be available for the use of the American physician. F. R. P.

Patologia e Terapia della Orecchio e delle Prime vie æere (Otologia, Rhinologia, Laringologia). Dr. Giuseppe Gradenigo. Torino: S. Lattes & Co., Librai Editori, 1903.

This large volume presents in the form of lectures the teachings of Gradenigo, the distinguished professor of laryngology at the University of Turin. Although intended primarily for the use of students, it is written with almost Germanic thoroughness, and consequently possesses value for the more advanced workers in laryngology and otology. Scientific medicine has in recent years been greatly benefited by the activity of the Italian profession.

The present work conveys the teachings of the most prominent Italian authority on laryngology and otology. The marginal notations which are to be found on every page are of great service as guides, especially to the reader who is not a fluent Italian student.

Although, as stated before, the book is of a more or less elementary character, it would nevertheless be of value to all workers in this special field if for nothing else because of the originality of many of the author's views upon important subjects. The great tendency in the American medical profession is to confine their researches in medical literature to works published in English, German, and occasionally French. Of course, this is owing to the fact that but few American physicians are sufficiently familiar with the Latin tongues to acquaint themselves with publications in Italian or Spanish. The converse of this proposition is, however, not true in the book at present under discussion, the references in which are of the most polyglot character, the author evincing familiarity with the medical literature of all tongues. F. R. P.

THE CARE OF THE BABY. A Manual for Mothers and Nurses. By J. P. CROZER GRIFFITH, M.D., Clinical Professor of Diseases of Children in the Hospital of the University of Pennsylvania. Third edition, thoroughly revised. Philadelphia, New York, and London: W. B. Saunders & Co., 1903.

THE appearance of a third edition of Dr. Griffith's well-known manual is a satisfactory indication of the favor with which the earlier editions have been received. In its present form it has been submitted to a thorough revision, a large number of illustrations have been added, and a few to which objection had been raised have been omitted.

While primarily intended as a popular book for the guidance of mothers and nurses, it contains a large amount of material that should be a part of the equipment of every physician whose work brings him into frequent contact with childish patients. It therefore offers an excellent primer for the student, inasmuch as every young practitioner is early brought face to face with baby patients; and it behooves him to be well prepared to face with confidence the discriminating criticism of the experienced mother and her gossipy friends.

Throughout the whole work the author aims to discourage overconfidence in the mother, and seeks to teach her what not to do for her child in case of illness rather than to assume responsibilities which should properly be relegated to the physician. It is therefore a safe book to put into the hands of mothers and nurses, and should prove a valuable adjunct to the nursery. T. S. W.

SERUM THERAPY. By R. T. HEWLETT, M.D., D.P.H. LOND. Philadelphia: P. Blakiston's Son & Co.

THIS small work of two hundred and fifty pages contains a concise account of the treatment of disease by antitoxins and antisera, with a brief description of the preparation and administration of these materials, the way in which they are supposed to act as curative agents, etc. Ehrlich's side-chain theory is clearly set forth and a chapter is devoted to transfusion of animal blood, saline solutions, and artificial sera. Those interested in this subject will find the book useful and quite complete for its size. T. A. C.

THE MEDICAL EPITOME SERIES. AN EPITOME OF INORGANIC CHEMISTRY AND PHYSICS. By A. MCGLANNAN, M.D., of the College of Physicians and Surgeons, Baltimore. Series edited by V. C. Pedersen, M.D. Philadelphia and New York: Lea Brothers & Co.

THIS small volume contains an excellent epitome of the most important facts in physics and inorganic chemistry. It will prove of special value to undergraduate students of those subjects, but will be a most serviceable companion to more advanced scholars who desire a résumé for handy consultation. To the medical man a book of this kind is a most useful little work of reference for consultation in some of the points which come up so frequently in his practice in relation to the sciences with which it deals. The plan upon which the matter is arranged is most practical. It is a pity that in the proof-reading a number of errors have been overlooked. They are not, however, of great importance, and do not in any way mar the accuracy of the scientific facts set forth.

E. A. C.

THE MEDICAL EPITOME SERIES. NORMAL HISTOLOGY. A MANUAL FOR STUDENTS AND PRACTITIONERS. By JOHN R. WATHEN, M.D. Philadelphia and New York: Lea Brothers & Co.

THE qualities that distinguish the Medical Epitome Series and which have made it justly popular are conspicuous in the present member of the group. It presents the same judicious arrangement of subject-matter, clear and concise language in the letter-press, with an adequate number of engravings selected from authoritative text-books, and the same continuity in the text in place of the fragmentary method of questions and answers of the older "quiz compends." The manual is as compact as it could be made without

sacrificing comprehensiveness, and is especially adapted to the needs of those for whom it is designed—students and practitioners confronted with the necessity of "getting up" knowledge on short notice when time is an important factor. R. M. G.

THE MEDICAL ANNALS OF MARYLAND, 1799–1899. Prepared for the Centennial of the Medical and Chirurgical Faculty. By EUGENE FAUNTLEROY CORDELL, M.D. Baltimore, 1903.

THIS volume, which was published as a commemoration of the Centennial of the Medical and Chirurgical Faculty of the State of Maryland, is a contribution of the greatest importance to the history of American medicine. Its author has long been distinguished for his labors in the field of American medical history. Had it not been for his zeal for research the immensely important part played by the profession of Maryland in the development of medical science in this country would hardly have been appreciated. There are indeed few States which can boast of a prouder record in this respect than Maryland. In this volume its claims are well presented. The work is divided into three sections, namely, an historical, a biographical, and a chronological section, the first portion being devoted to a history of the Medical and Chirurgical Faculty, the second to biographical sketches of its members, and the third to a chronological record of events of importance in the medical history of Maryland. The Medical and Chirurgical Faculty of Maryland for many years occupied a peculiarly important position in the fact that until the year 1859 physicians desiring to practise within the limits of Maryland were obliged to have a license from it. In that year this power was taken from it by legislative enactment.

In the chronological record we would note that in all probability the autopsy stated as having been made in that colony in 1637 is the earliest recorded in America, and in addition there are also a number mentioned subsequently, all of which were performed prior to the autopsy performed in Massachusetts in 1674, and very generally supposed to have been the first.

Another "first event" is noted in the year 1768, when John Archer, of Maryland, received the first medical diploma, "M.B." from the University of Pennsylvania, ever granted after attendance in America. In more recent times, the first annual meeting of the American Medical Association was held in Baltimore in 1848. Many other interesting facts might be quoted from this well-compiled record did space allow.

Among the biographical sketches are several of the greatest interest and value, dealing with the early celebrities in the profession, many of whom have not so far been brought adequately before the

public. Among these may be mentioned those of Upton Scott, John Archer, John Crawford, and Horatio Gates Jameson.

Dr. Cordell's book is one of the greatest interest not only to the physicians of Maryland, but to those of the whole United States. It is an excellent example of what should be done in various localities to gather up as much of the local medical history as possible, and preserve it before it is irretrievably lost. F. R. P.

A Text-book of the Practice of Medicine. By James M. Anders, M.D., Ph.D., LL.D. Sixth edition, thoroughly revised. Philadelphia, New York, and London: W. B. Saunders & Co., 1903.

The appearance of the sixth edition of this work in six years in itself attests its popularity among students and practitioners. The work has been revised and brought up to date, as has become necessary in those diseases where information is rapidly accumulating. In addition new diseases or symptom groups have been introduced.

The author has made use—as in former editions—of a tabular parallel in differential diagnosis of diseases which present like symptoms. Many of these tables are original with the author. Of the new subjects introduced are paragraphs on paratyphoid fever, the fourth disease; trypanosomiasis, orthostatic albuminuria, transcortical aphasia, adiposis dolorosa, and amaurotic family idiocy.

In a work of such general excellence it is difficult to pick out any particular portion as deserving of special notice. The chapters on Tuberculosis, Diseases of the Heart, Anæmias, Malaria are very complete reflections of our present knowledge of these subjects, and the same statement applies to the book *in toto*. The author has a very clear method of expressing himself and does not overload us with facts in support of theories already proven and accepted. Also, in discussing diseases of unknown or disputed etiology and pathology, both sides of the question at issue are given and not too much weight placed on an individual opinion. As an illustration of this method of treatment, the chapter on Diabetes may be cited.

Dr. Anders has been aided by others in revising the parts on the Nervous System and some of the section on Children's Diseases, and this work has been done in the same thorough way. The combination of careful methodical work, of studying and making use of current medical literature, with the author's own wide experience, has made this a standard text-book second to none.

J. N. H.

PROGRESS

OF

MEDICAL SCIENCE.

MEDICINE.

UNDER THE CHARGE OF

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The Measurement of the Pressure in the Right Auricle (a New Clinical Method).—GUSTAV GAERTNER (*Münchener med. Wochenschrift*, 1903, No. 47). Gaertner's method depends upon the well-known fact that when the arm hangs by one's side the veins fill with blood, which empties out when the arm is raised. This Gaertner calls the "vein phenomenon." It occurs normally when the vein to be tested in the arm is raised to the level of the costal insertion of the third, fourth, or fifth rib. Gaertner argues that the occurrence of the "vein phenomenon" is dependent upon the pressure in the right auricle. The veins form manometers, which, although not transparent, indicate the position of the blood column. A slight positive pressure suffices to distend their walls, while they collapse if the pressure is zero or negative.

He recognizes two limits: 1. The elevation of the arm at which emptying of the veins just occurs. 2. The elevation of the arm at which the veins just do not collapse. Of these only the first is important. The pressure in the right auricle is measured by determining the vertical distance between the level of the right auricle and the level of the vein examined. The pressure in the right auricle is subject to rhythmical variations. It rises during systole and sinks during diastole, and varies with inspiration and expiration. The veins of the arm constitute, as it were, a "minimum manometer."

By adjusting the arm at the proper height, Gaertner observed pulsation in the veins in cases of mitral disease, and in cases of dyspnœa. A voluntary increase of pressure in the right auricle can be produced by forced expiration when one holds the nose (Valsalva experiment).

He found that the pressure in the veins is not identical with the pressure in the thorax. By increasing the pressure in the thorax artificially to the equivalent of 10 cm. of water, the pressure in the auricle rose only about 6 cm. With an increase of 15 cm. in the thorax the auricular pressure rose only about 11 cm. He noticed the curious fact that negative pressure in the thorax produced no diminution, but actually an increase of pressure in the auricle.

Gaertner had an opportunity to test the pressure in a number of patients in Prof. Neusser's clinic.

His experiments showed that in all cases, without exception, in which there was congestion of the right heart he was able to demonstrate by his method an increased auricular pressure. The difference from the normal was naturally dependent upon the nature of the case. In almost all cases it was so material a difference as to be readily recognized. Usually in healthy people the veins collapse when the hand is at or below the level of the shoulder; some cases when it is raised to the level of the eye or top of the head. He designates the auricular pressure as V. D. (Vorhofsdruck). He took as his standard the upper border of the fifth rib. He found that the pressure varied from 9 cm. to 23 cm. In the case of pericarditis about 20 cm., in lung emphysema about 18 cm., in lobar pneumonia 29 cm. He found also increase of pressure in tuberculosis, pleural exudation, and so on. The highest pressure was 37 cm. in an individual with beginning infiltration of the apices of the lungs. In this last case a satisfactory explanation of the pressure was not found.

He records the varying changes of pressure in the infarct of the lungs that was observed very early.

At times the increased auricular pressure was the only objective symptom that indicated damaged circulation. In one case the pressure was 20 cm. in a woman, aged about forty years, in whom the investigation of the heart and lungs gave no signs of disease. Clinical history, however, showed that there was cardiac insufficiency.

In describing his method, Gaertner suggests that changes may be required after further experiences. The determination is best made with the patient sitting upright. The back should be supported in order to prevent alterations of the position during the determination. With fat people or with those with abdominal tumors, ascites, etc., the feet should rest on the ground, since when sitting in bed the abdominal pressure produces circulatory changes. Thin patients could be measured even while sitting in bed. The anterior plane of the thorax should be as upright as possible. In semirecumbent position the determination is more difficult. The chief difficulty occurs when one attempts to determine what point must be selected as the normal zero point. At first he was inclined to select the upper limit of heart dulness; but he later concluded to select a point on the skeleton, and chose the sternal insertion of the upper border of the fifth rib. This is easily demonstrable, and there can be no question of its position, while there might be controversy about the limits of cardiac dulness. Furthermore, this point corresponds in healthy human beings to the level of the tricuspid valve. Finally, the horizontal plane that passes through this point is to be regarded, according to his observations, as the lowest limit at which the vein phenomenon occurs. In all cases, then, one will obtain a positive value for V. D., while if a higher point be selected the value for V. D. may be either positive or negative. It may be said that the auricle in diastole forms a space 6 cm. to 8 cm. in vertical measurement, so that in the auricle itself there must be differences of pressure according as the measurement is at the top or bottom of the auricle, and by selecting the lowest point of the auricle, that is, the tricuspid valve, as his zero point, he always obtains a positive value for his auricular pressure.

Having determined that one will select the lowest plane of the auricle for the measurements, it remains to determine where this lowest point falls. It would be simple to determine this matter by means of

Roentgen-ray pictures, but this is a complicated procedure. For practical diagnostic purposes such exactness is superfluous, for in pathological cases the extent of the pressure is so far from the normal that it is readily perceived by less exact means.

Of the veins that may be selected for examination, those of the back of the hand and the radial surface of the forearm are the most suitable. At times these are not available, and any vein that presents must be selected, such as the median basilic. It is rare in adults that no vein occurs available for this determination, though this is common among well-nourished children.

Under the action of cold the veins become invisible; the use of warmth in any form, however, quickly restores the circulation to the skin and brings out the veins. One must select a vein that collapses readily. On the backs of the hands of old people it is not uncommon to find thickened varicose veins which do not collapse. Exceptionally, such veins occur also on the forearm and upper arm. The collapse of even the most delicate vein is sufficient for the determination. A good illumination and a suitable position of the observer are essential for this. If the eye of the observer is a little bit higher than the vein and if the light comes over the shoulder of the observer, one can see the shadows cast by the rising vein over the congested skin and can determine the moment of collapse by the disappearance of the shadow. Of course, one must be careful that articles of clothing do not interfere with the circulation and must be sure that the handling of the arm does not occlude any of the veins. The person examined must not hold his breath; the arm examined must not be too sharply bent at the elbow, at the most about 120 degrees; nor should the arm be everted from the shoulder.

Before beginning the final determination, let the arm hang vertically and wait until the blood column accumulates to the shoulder after two or three minutes. Then bend the arm, held in adduction to an angle of 120 degrees at the elbow and pronated. The forearm must be raised from the shoulder so that the whole forearm stays horizontal. In this case the collapse occurs simultaneously in the whole extent of the forearm. The movements must be executed by the physician with care not to compress the vein. The muscles of the person examined must be as relaxed as possible. Several determinations must be made, preferably using both left and right arms. Often the first determinations are higher than the later ones, as the patients are frequently somewhat excited by the examination. Once Gaertner observed a very great increase of pressure after only very slight muscular exertion in the case of a patient with mitral disease. The determination of the difference of level between the auricle and the observed vein can be either approximate or accurate. According to the first method, one roughly measures the height of the vein at the point of emptying and projects it upon the median plane of the body, and in this way finds how much above the given zero point the collapse occurs. It is much more accurate to measure this pressure in centimetres, which Gaertner does with a simple apparatus that he describes.

The first objection that may be raised is that he is obtaining hydrodynamic relations and not hydrostatic, and second that the pressure in the peripheral vein is modified by a suction action where the small vein empties into the jugular. Third, that the elasticity of the vein walls modifies the result.

He also made determinations using the veins in the foot and leg

He thinks that a comparison of the results given on the upper and lower extremities gives us a means of determining intra-abdominal pressure. His conclusions are as follows:

1. An observation of the "vein phenomenon" puts us in a position to determine the pressure in the right auricle in a manner beyond objection, as far as the laws of physics are concerned.

2. By means of the method here described we can recognize the presence of congestion in the right heart not only with certainty, but actually can measure the degree of injury and follow the course of alterations. We will be able to follow very accurately the limits of therapeutic measures.

3. The method is so simple, the appearance is so unmistakable that its application will recommend itself for diseases of the circulation and respiratory organs.

Oskar Prym (*Münchener med. Wochenschrift*, 1904, No. 2, p. 60) raises several objections to Gaertner's method which was recently proposed. Having tried this method repeatedly in the clinic at Bonn, he finds: 1. The vein phenomenon occurs in the same individual at unequal heights in different veins; the difference amounted to 6 cm. or 8 cm. or more. 2. There was often a rapid change in the height at which the vein phenomenon occurred, which depended apparently upon the rapidity with which the arm was raised. With more rapid raising of the arm the vein phenomenon occurred at a greater height. 3. On account of the influence of varying pressure and varying volume of blood passing through the veins, and on account of the varying tonus of the veins, he concludes that the vein phenomenon does not always indicate either the lowest pressure in the right auricle nor the highest pressure. The vein phenomenon may indicate either too high or too low a pressure. He thinks it not allowable to regard the veins as simple manometers, for the height at which the vein empties is dependent not only upon the pressure in the right auricle, but also upon the amount of flowing blood, upon the resistance to the outflow, and upon the tonus of the vein. He thinks that Gaertner's method may be of use clinically if these factors are borne in mind.

SURGERY.

UNDER THE CHARGE OF

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The Treatment of the Congenital Dislocation of the Hip.—Reiner (*Centralblatt f. Chir.*, 1904, No. 2) considers this subject under two separate headings: first, radical treatment in relation to the age of the patient, and, second, the after-treatment. The method of Schlesinger,

of Dresden,-consists in reduction followed immediately by immobilization in a plaster cast, but we must remember that he states that three years is the age limit for this procedure. Reiner has found, however, that this method may be tried up to the twelfth year where both sides are involved, and to fifteen years in the single variety. In patients of this age the idea should be not to accomplish complete reduction at the first sitting, but instead to merely bring the head of the femur near the articular surface of the acetabulum. The reduction should then be completed in from eight to fourteen days, and in 12 cases the method was successful. In regard to the after-treatment, active and passive motion are essential, care being taken to see that reduction is absolute at the end of the movement.

Intracapsular Resection of the Prostate for Hypertrophy.—RYDYGIER (*Centralblatt f. Chir.*, 1904, No. 1) states that there have lately appeared three articles on the subject of the treatment of prostatic hypertrophy by Riedel, Zuckerkandl, and Völcker; Riedel not only goes into the technique, but also into the operative indications, and his conclusions are in the same line with those of Rydygier, who, however, does not agree with Zuckerkandl and Völcker. The author notes that in 1900 he fully described partial perineal prostatectomy and also in 1901 and 1902 the intracapsular operation as related to resection, but Zuckerkandl evidently did not come across these references, for at one place in his article he notes his priority in this field of work. The author's method differs from those of Alexander, Nicoll, Jabulay, Freyer, and others; also from Czerny, which Völcker describes, and from Zuckerkandl. As this condition usually exists only in men who are senile, the author's idea is to make the operative interference as slight as possible so as to avoid shock. The technique consists in making an incision in the raphé of the perineum, then separating the capsule to one side about 1 to 2 cm. from the median line in a longitudinal direction. The urethra should not be opened as Zuckerkandl advises, as no advantage is gained by doing so. Total extirpation is certainly not necessary in every case and it is far more dangerous than a partial reduction. Care, too, should be taken not to injure the rectum as happened in several of Zuckerkandl's cases, and also not to injure the ejaculatory ducts. That recurrence is more common after resection than after other methods does not seem probable; the operation should be performed in the early stages of the disease, and it is one that is but very slightly dangerous and which should not be followed by disagreeable sequelæ.

Some Practical Points Associated with Appendicitis.—SPANTON (*British Medical Journal*, February 6, 1904) states that the early symptoms are often not only obscure but positively misleading, and the typical signs the books describe so mathematically are often represented by a cipher. The author then reports 10 cases in detail and remarks that the ordinary symptoms of simple appendicitis are sufficiently familiar and so need not be detailed here. But there are some to which undue importance is attached, while there are others which may readily be mistaken for those of other morbid conditions. Pain, for example, is relied upon by some as essential, but in several of the cases the pain was so slight as to be hardly mentioned by the patient.

The locality of the pain, too, is very misleading. In a large proportion of the worst cases the pain is referred to the epigastrium or along the course of the colon. Epigastric pain is almost invariably associated with peritonitis and is one of the most valuable indications of its presence and the need for operation in these cases. Tenderness on pressure and referred pain should be kept distinct. Tenderness is usually over the seat of the appendix, but it must be borne in mind that the appendix may be fixed in one of the hernial openings (it occupied the obturator foramen in one case) or, on the other hand, it may be free and move its position considerably; hence the location of the tenderness may vary greatly. In women it is liable to be confounded with ovarian tenderness, and it is not an uncommon thing for the appendix and ovary to be adherent—both inflamed—and the author has elsewhere pointed out the comparative frequency of appendicitis in young women occurring at the catamenial periods. The presence of a lump is again very misleading, for a good proportion of such cases without very marked constitutional symptoms do well and recover without operation, while, on the other hand, the absence of such a swelling indicates little, for the appendix may be gangrenous, may be hidden away down in the pelvis, or may be doubled down behind the ileum, in which cases no lump would be perceptible.

But when we come to abdominal tension, especially with rigidity of the right abdominal muscles, we have an indication of a more definite character, almost always denoting formation of pus or circumscribed peritonitis, which in conjunction with constitutional symptoms, especially persistent sickness, is almost pathognomonic. In such cases operation is demanded. Constipation is no doubt usually present, but, on the other hand, spurious diarrhœa is not uncommon. There is frequently a history of more or less habitual constipation, with some unusual meal followed by sickness and diarrhœa, which may persist even as the graver symptoms increase. Temperature counts for little, except when a sudden rise gives indication of grave mischief, which is ordinarily apparent enough already. The same as to pulse; it is often quiet and even slow when the necessity for operation is clear enough. The necessity for operation must be judged on the merits of each individual case, but it is far safer to operate too soon than to defer it a minute too long. A certain proportion of patients will get well with ordinary care and treatment, especially strict recumbency; but in all cases of doubt it is far safer for the patient and more to the credit of surgery to act soon, and make practically certain of saving the patient's life. No one ought to be allowed to die unopened unless practically moribund, and some most desperate cases do get well.

Notes on the Ineffectual Treatment of Cancer.—POWER (*British Medical Journal*, February 6, 1904) states that in cancer, with its apparently increasing mortality, it is only right that a fair trial be given to every method of treatment which promises to give relief, provided that the method can be adopted without ill consequences to the patient. With this end in view, three cases were treated by the injection of the Schmidt serum; one, a woman, from whom had recently been removed a part of the breast for a scirrhous carcinoma; a man, the half of whose tongue had been removed for epithelioma, and a patient from whose neck had been removed a malignant growth the origin of which

was not clear. After noting in great detail the progress of each of these cases the author states in conclusion: 1. In regard to the reaction. There is no doubt that a reaction takes place after the injection of Schmidt's serum. The temperature rises and with it the pulse, but the respirations as a rule are not affected. In this rise of temperature there was nothing peculiar, for it follows the injection of serum which admittedly contains toxins and in all probability any similar serum would produce a similar result if it were active. It cannot therefore be said with accuracy that the reaction is specific, and this is proved by the fact that the first case showed the most typical reaction, yet subsequent examination of her tissues failed to detect any malignant disease. 2. The local effect upon the tumor was shown in each case, for the breast in the first case and the malignant masses in the other two cases became inflamed and reddened as the result of the injection. Yet here again one could not see that the serum acted by selection upon malignant tissues only. It seemed to intensify any pre-existing inflammation. This was effectually shown in the first case, where the lymphatic glands in the right axilla became enlarged in addition to those in the left armpit, the original seat of cancer being the left breast. For here again subsequent examination showed that none of the glands which had thus become enlarged after the injections of the culture were affected with cancer. 3. The treatment is certainly painful apart from the succession of hypodermic injections.

Lastly, malignant disease progresses even to a fatal issue while the injections are being given, as happened in the second case. The author believes that this method is of no service at present, either from a prophylactic, diagnostic, or curative standpoint, but it may fairly be argued that this trial has been insufficient and that further observations are desirable.

THERAPEUTICS.

UNDER THE CHARGE OF

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Mineralization and Hypochloruration in the Bromide Treatment of Epilepsy.—M. TOULOUSE considers that hypochloruration aids materially the action of the bromides in the treatment of epilepsy, but it causes a demineralization of the patient, who is thus rendered more liable to infection, especially that of tuberculosis. To remedy this, sodium chloride is replaced by sodium phosphate. Five patients were treated by the administration of 75 to 150 grains of sodium phosphate per day. No crises occurred. It seems rational to admit that sodium phosphate does not interfere with the absorption of the bromides. A diet rich in chlorides seems to create, on the part of the tissues, a desire for homologous salts, such as the bromides. The author's experiences confirm the theory of modifying the nutrition in order to augment the action of drugs.—*La presse médicale*, 1904, No. 11, p. 86.

Radium in Certain Nervous Affections.—M. A. DARIER has succeeded in two cases in terminating neurotic convulsive attacks which had in one patient been accustomed to occur every day, and in the other three or four times a week, by applying tubes containing radium to the temples. Also in a case of neurasthenic pseudo-ataxia and in a case of recent facial paralysis, cure resulted after a day's application of the radium. The activity of the radium employed varied from 10,000 to 7000 units, and the feeble intensities were applied for three or four days or even up to fifteen days, pain appearing a short time after the cessation of the application. With intensities of from 1000 to 7000 units the duration of the sittings was from two to six hours per day.—*La semaine médicale*, 1904, No. 7, p. 51.

Solanum Carolinense in Epilepsy.—DR. TRUSCH, after a study of this drug, has arrived at the following conclusions: 1. That solanum carolinense possesses great value in the treatment of idiopathic, non-hereditary *grand mal*, especially when the disease begins after childhood. 2. That it is also very useful in hystero-epilepsy with convulsions; in *petit mal* its effect is less marked. 3. In advanced epilepsy, where cell degeneration in the brain seems to have been established, the drug seems to have an almost specific action, but its effect does not last so long as does that of the bromides. 4. The author's observations show that the vegetable depressomotors possess real advantages over the mineral salts employed to produce this effect. With solanum the bad effects of the continued use of the bromides are avoided, especially the dermatoses and the influence upon the mind. 5. The fluid extract of the drug seems to be the preparation to be preferred.—*Journal de médecine de Paris*, 1904, No. 8, p. 74.

Intravenous Collargolum Injections in Septic Affections.—DR. GEORGE TUCKER HARRISON reports a case of pyæmia following criminal abortion which, when first seen, had a weak pulse, remittent temperature, effusion in the right knee-joint, and a gluteal abscess. After the first injection of collargolum in twenty-four hours the pulse and temperature were nearer to the normal and the general condition was much better. Two more injections were given during the following three weeks, but the fever continued because of an abscess which developed in the right thigh. This was incised, drained, irrigated, and dressed. On the following day not a drop of pus was present, and recovery rapidly ensued. The author remarks this as being unusual in such cases, and reports a case of puerperal sepsis, and, in conclusion, states that he has seen no such brilliant recoveries as those following the use of collargolum.—*Virginia Medical Semi-monthly*, 1904, No. 20, p. 477.

Epidural Injections in Genito-urinary Diseases.—DR. ARTUR STRAUSS reports his results in 18 cases of various genito-urinary disorders. Of 10 cases of enuresis, 1 was cured by an operation for phimosis rather than by the injections, in 2 the enuresis by day was cured, while that of the night was improved; 5 others were also improved, while 3 passed out of observation. Two cases of incontinence were cured. Of 7 cases of pollution all were cured, while of 3 of spermatorrhœa 2 recovered, while the third was unimproved. One case of prostatorrhœa and 2 out of 3 cases of impotence were cured, while of 2 cases of neuras-

thenia sexualis 1 was improved, while the other remained *in statu quo*. The author used for injection at first 0.2 per cent. sodium chloride to each 10 c.c. of which 2 drops of 5 per cent. carbolic acid had been added; later Schleich's solution was used. From 10 c.c. to 35 c.c. were injected into the lumbar sacral region of the cord at each sitting, and, in the author's opinion, the operation, when done under strict asepsis, is not in the least dangerous. The indications for its performance seem to be: infantile eneuresis, incontinence without mechanical obstruction, emissions, impotence, spermatorrhœa, and neuropathic polyuria.—*Therapeutische Monatshefte*, 1903, No. 2, p. 74.

Treatment of Tuberculous Meningitis by Lumbar Puncture.—Dr. H. Serafidi has treated three patients suffering from this affection by lumbar puncture with the following results: The first patient, aged nine years, when seen was in the position of opisthotonos, with photophobia, frequent emesis, etc., and a pulse of 160 per minute. On the fourth day of the disease 10 c.c. of fluid were drawn off by lumbar puncture, and amelioration began at once. In three days recovery was assured. The second patient, aged fifteen years, exhibited practically the same symptoms as the first. On the eighth and ninth day of the disease lumbar puncture was performed. The patient's condition rapidly improved and a few days later he was entirely well. The third patient, aged one and a half years, presented classical symptoms of the disease, and upon the fourth day of the illness 10 c.c. of clear fluid were drawn from the spinal canal. Slight improvement followed, and two days later 34 c.c. of fluid more were withdrawn. Recovery followed without event. The author states that if any conclusion can be drawn from these three cases it is that the cure of tuberculous meningitis is not absolutely impossible. He considers these recoveries permanent, since considerable time has elapsed.—*Revue de thérapeutique*, 1903, No. 3, p. 80.

Secretine.—M. Ed. Enriquez, who has made extensive experiments with this substance (which is an acid extract prepared by macerating the duodenal mucous membrane), has demonstrated that it is not exclusively an excitant of the pancreatic secretion, but that it increases also the flow of bile, and that the result of introducing an acid substance into the duodenum and that following the injection of secretine into the circulation are identical. Seven patients in whom the dominant symptom was habitual constipation were treated by the author, with the result that the motor and secretory functions of the intestine were stimulated and regular evacuations of the bowel were obtained. Of five cases in which the constipation was accompanied by the symptoms of mucomembranous colitis, such as painful abdominal crises and passages of mucus, four were relieved of the constipation, and at the same time the other symptoms were rendered much less distressing. Of four patients in whom the constipation was associated with lack of motility of the stomach, delayed digestion, and general lassitude, all were favorably and rapidly affected by the treatment. In conclusion, the author states that the acid duodenal medication has an undoubted stimulant action upon secretion, and since it increases the quantity of bile and pancreatic juice and also excites the motility of the intestine, it should prove of considerable value in intestinal dyspepsias.—*La presse médicale*, 1903, No. 14, p. 106.

PEDIATRICS.

UNDER THE CHARGE OF

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OF PHILADELPHIA.

A Simple Method for Obtaining Sputum in Children.—LEONARD FINDLAY, of Glasgow (*Archives of Pediatrics*, February, 1904, p. 126), referring to the difficulty experienced in obtaining specimens of sputum from young children, describes a method which has been in use for years in the French hospitals, but which he has not found described in any English work. It consists in irritating the pharynx and especially the epiglottis with the forefinger wrapped with a piece of gauze; cough is thus excited, and any expectoration that is coughed up is swept out of the mouth by the finger before it has time to be swallowed. The quantity thus obtained varies, but, as a rule, is sufficient for bacteriological examination. Several attempts may be required, but even in children as young as six months sufficient has been obtained on which to found a diagnosis. This method he has practised as a routine measure for nine months in the Royal Hospital for Sick Children, Glasgow, and with very gratifying results. Many cases of not very well-marked tuberculosis of the lungs were diagnosticated early, even on the day of admission to the hospital, and, with only one exception, no case of pulmonary tuberculosis went to post-mortem examination without the tubercle bacillus having been found in the sputum at some time. In cases of meningitis, also, supervening upon local pulmonary disease, in which there was a doubt as to its being tuberculous or pneumococcic in origin, the finding of the tubercle bacillus in the expectoration removed in the manner described cleared up the diagnosis.

Impetigo and Ecthyma Showing the Diphtheria Bacillus.—RAOUL LABBE and DEMARQUE, of Paris (*Revue mensuelle des maladies de l'enfance*, February, 1904, p. 49), report two cases in young children exhibiting extensive lesions of impetigo and ecthyma, in which were found, besides staphylococci in one case and staphylococci and streptococci in the other, various forms of Klebs-Loeffler bacillus. The same organisms were found in the throats of the patients, and both received injections of Roux's serum (20 c.c.), although no clinical symptoms of faucial diphtheria were observed, and no history of previous sore throat could be elicited in either case. The cutaneous lesions resembled those of a staphylococcic infection, but differed in their slow and chronic evolution. Without doubt, such cases are not exceptional, but the authors have failed to find reference to similar observations in the literature. They advise recourse to bacteriological examination of all cases of impetigo or ecthyma with multiple localizations in children, and that serum should not be neglected as one of the culture media. In

such cases serotherapy should be employed early, but local treatment should not be neglected, and here, probably, the method of topical application of antidiphtheritic serum recently suggested by L. Martin (*Comptes-rendus soc. de biologie*, May 16, 1903) may find an appropriate field.

The Open-air Treatment of Bronchopneumonia Complicating Whooping-cough.—KER (*Scottish Medical and Surgical Journal*, January, 1904) gives the results obtained in the treatment of the complicating bronchopneumonia of whooping-cough by the open-air method, as practised at the Edinburgh City Hospital.

The writer calls attention to the high death rate from this disease, especially among the lower classes and in children living in institutions, and to our helplessness in its treatment.

Although much can be done to secure the patient rest and to maintain his strength, the practical point is some method of successfully treating the bronchopneumonia, which is the cause of death in the vast majority of cases.

The records of the Edinburgh Hospital show a death rate of 71 per cent. for the cases with bronchopneumonia, and statistics from other hospitals give about the same results.

The fact that many of the whooping-cough patients developed bronchopneumonia after admission, evidently from ward infection, influenced the writer to try the open-air treatment. At least any method, however heroic, could hardly increase the death rate.

Many writers have recommended that children suffering from pertussis be allowed out in the open air, but the occurrence of a pulmonary complication is usually said to be a contraindication of this treatment.

The first cases were selected from the worst in the wards, and many of them were regarded as hopeless. They were carried out and left in the open air for about six hours daily, provided it did not rain. No bad results were noted, and there was a very marked improvement in some of them. The children were warmly covered, and the chest was protected with cotton. The main effects of the treatment were as follows: The whoops were unaffected in number or severity. The patients took their food ravenously, and their general strength was improved. They also slept better, and the whole nervous tone of the children was improved. Another practical advantage was the complete rest given the wards for a period of from one to seven hours daily. While one case, which was admitted uncomplicated, developed bronchopneumonia and several had relapses in convalescence, it may be said that under this treatment bronchopneumonia of hospital origin became extinct. As regards the severity of the cases treated there is no doubt at all. Many were admitted cyanosed, with temperatures of 103° F. or 104° F., respirations of 60 to 80, and pulse running from 140 to 170. Even in the favorable cases these symptoms continued for a long time, though the pulse and respiration rate slowly decreased and the cyanosis disappeared.

The writer gives tables of various groups of cases treated over certain periods, the results of which are briefly stated as follows: Treated indoors entirely: cases, 74; deaths, 51; death rate, 66.9 per cent. Treated outdoors partly or entirely: cases, 76; deaths, 24; death rate, 31.5 per cent.

Pyelitis Due to the Bacillus Coli Communis.—McCay (*Indian Medical Gazette*, December, 1903) reports a case of pyelitis in a child, aged seven years, the true nature of the infection not being discovered until the patient had been under treatment for several weeks. The child was taken ill suddenly with pain in the left side extending down the leg. There was tenderness over the left lumbar region, coated tongue, constipation, and a temperature of 101° F. A week after the onset the temperature had risen as high as 105° F., with marked remissions. Pus was suspected, but could not be localized. The urine at this time was acid, with a trace of albumin. There was some abdominal distention, and constipation was a prominent symptom. The case was then thought to be possibly atypical typhoid fever. The patient continued to have high, irregular fever, accompanied by chills and vomiting, and when seen by the writer for the first time was extremely weak, anæmic, and much emaciated. There was œdema of the forehead and below the eyelids.

The blood examination gave a negative Widal reaction, while the urine showed a moderately large quantity of pus and abundant lively colon bacilli. The patient was given citrate of potassium in large doses, which had the effect of rendering the urine alkaline and of diminishing the amount of pus, but had no influence upon the bacilli. They grew rapidly on the various media and were very mobile. Urotropin was then given, and at once the bacilli, to a certain extent, lost their motility, and the number of colonies were fewer. After a few days they had entirely disappeared from the urine. The patient made a rapid recovery.

GYNECOLOGY.

UNDER THE CHARGE OF

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Changes in the Endometrium in Ectopic Gestations.—Cazeaux (*Annales de gyn. et d'obstétrique*, Feb., 1904) arrives at the following conclusions: The expulsion of a complete membranous cast of the uterine cavity in ectopic gestation is not constant, nor does it imply the death of the fœtus. It has not been proved that this occurrence signifies some disturbance at the site of the ovum. This cast is formed by the superficial layer of the mucous membrane of the uterus, and the line of separation is never beyond the limits of the ampulla.

Function of the Corpus Luteum.—Labusquiere (*Annales de gyn. et d'obstétrique*, Feb., 1904) concludes from a study of Fraenkel's work and from his own observations that the corpus luteum is a true ovarian gland which is renewed regularly and affects the nutrition of the uterus and the periods of puberty and the menopause. It is not the pressure

upon the nerves of the ovary by the growing follicles that excites the menstrual flow, but the activity of the corpus luteum, since the latter presides over the periodical hyperæmia of the uterus which terminates in either menstruation or pregnancy.

Direct Illumination in Gynecology.—D. DE OTT (abstract of monograph in *Annales de gyn. et d'obstétrique*, Feb., 1904) advocates the general application of electric illumination in gynecological examinations and operations, using a number of simple appliances which are clearly figured and explained in his original *brochure*. A suitable head mirror is worn by the operator during abdominal and vaginal cœliotomies, the patient being in the exaggerated Trendelenburg posture on a special table.

Examinations of the rectum and bladder are similarly conducted, the interior of the latter viscus being exposed by separating the opposing surfaces of the urethral and vesical sphincter by means of small retractors, instead of with an endoscope. One blade of the retractor carries an electric light.

(The French editor properly calls attention to the fact that the advantages of extreme pelvic elevation during examination of the bladder were long ago recognized by American gynecologists, and that there is nothing new about the method of illumination.)

Torsion of the Pedicle.—HAMMER (Inaugural Dissertation; abstract in *Zentralblatt f. Gynäkologie*, No. 5, 1904) analyzes 43 cases of torsion of the pedicle noted in 248 ovariotomies at the Würzburg clinic. In 7 per cent. there were sudden colicky pains; in 60.5 per cent. several minor attacks were noted; 32.5 per cent. were unattended with symptoms, the condition being found at the time of operation. Torsion occurred in 32 cystoadenomata, 4 dermoids, 3 parovarian cysts, 1 fibroma, and 1 cystosarcoma. Twenty-three torsions were from left to right and 18 in the opposite direction.

The writer agrees with Hofmeier that unsymmetrical development of the neoplasm is the direct cause of the accident, pregnancy having little influence upon it. All the patients recovered but two, who were in collapse when admitted.

Late Recurrence of Mammary Cancer.—MARGGRAFF (Würzburg Inaugural; abstracted in *Zentralblatt f. Gynäkologie*, No. 5, 1904), in reporting a case of recurrence eight years after amputation of the breast for scirrhus, analyzes 860 cases in which the disease reappeared in 430 (50 per cent.). The longest period of immunity was eleven years.

(We have recently removed a recurrent cancerous nodule thirteen years after the primary operation.—H. C. C.)

Pathology of Uterine Fibroids.—WATT-KEEN (abstract of Inaugural Dissertation in *Zentralblatt f. Gynäkologie*, No. 5, 1904) in 417 cases from Hofmeier's clinic notes the following complications: ovarian cyst, 27; diseased tubes, 19; hernia, 7; uterine displacements, 14; carcinoma and sarcoma of the corpus uteri, 9. Myxomatous degeneration of the fibroid was present in 8 and necrosis in 8. Twenty per cent. of the married women were sterile.

Myomectomy (abdominal) was performed 123 times, supravaginal amputation 44, total extirpation 15. Forty-five vaginal myomectomies

and 43 total hysterectomies were performed. The total mortality after all operations was only 6.48 per cent.

Tuberculosis of the Tubes.—Fellenberg (*Zentralblatt f. Gynäkologie*, No. 5, 1904) reports 10 cases from the Bern clinic in which the diagnosis was confirmed microscopically. All the patients were nulliparæ; in none were there any characteristic symptoms, and no ulcerations were present on the vagina or cervix. The peritoneum was affected in two cases and the ovary only once, the uterus being free from disease in every instance.

The writer regards the prognosis after salpingectomy as generally favorable. In this respect he differs from those who advocate extirpation of the uterus and adnexa in every case of tuberculosis of the tubes.

Pruritus Vulvæ.—Lorand (*La policlinique*, vol. xii., No. 6) believes that diabetes is the etiological factor in the majority of the cases, and that it is frequently overlooked because the urine is not carefully and repeatedly examined, especially after giving test meals.

Three conditions may favor the development of pruritus in diabetes, viz.: 1. The toxic influence of the blood. 2. Direct irritation from the urine, which is rich in uric acid, as well as sugar. 3. Local hyperæsthesia of nervous origin. As regards treatment, the writer states that in addition to regulation of the diet he has obtained good results from the use of ointments containing 10 per cent. naphthalin and anæsthesin.

Torsion of the Omentum.—Vignard and Girandeau (*La policlinique*, vol. xii., No. 6) add 2 new cases to the 18 already reported. In both the symptoms warranted the diagnosis of appendicitis, the true condition being found only at the time of the operation. Of the 20 recorded cases 15 occurred in men and 5 in women. In all a hernia existed, so that this condition is evidently the principal etiological factor. The diagnosis is obscure and can seldom be made before operation. The treatment consists in resection of the affected portion of omentum above the point of torsion.

Deciduoma Malignum after the Menopause.—McCann (*British Obstet. and Gyn. Journal*, No. 3, 1903) reports the case of a woman, aged fifty-three years, who had borne ten children, the last nine years before. Menstruation had ceased a year and a half before she came under observation, complaining of profuse metrorrhagia of four weeks' duration. The patient succumbed on the sixth day after hysterectomy. Examination of the uterus showed the presence of a deciduoma malignum.

Vaccinia of the Female Genitals.—Löwenbach (*Monatshefte f. prakt. Dermatologie*, Band xxxvi.) states that he has observed four cases in which healthy women were infected on the genitals from individuals who had been recently vaccinated. He was able to find only one other similar recorded case. Infection took place through the medium of clothes, by direct contact, scratching, and in one instance because a physician who had dressed a vaccination sore on a child's arm made a vaginal examination of the mother without washing his hands. In the early stage the vesicle must be differentiated from pemphigus, eczema, and herpes, in the later stage from the syphilides.

OBSTETRICS.

UNDER THE CHARGE OF

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Diabetes Mellitus and Metritis.—LEIPMANN (*Archiv für Gynäkologie*, Band lxx., Heft 2, 1903) reports the case of a patient, aged thirty years, in her sixth pregnancy. The abdomen was more enlarged than the gestation warranted, heart sounds could not be heard, fetal movements could not be felt, and the patient suffered from dyspnœa. There was a history of diminution in the quantity of urine voided; the feet were swollen; the urine contained large quantities of sugar with a trace of albumin, with leukocytes, but no casts and kidney epithelia in the sediment. The membranes were ruptured and about eleven pints of amniotic liquid allowed to escape. The head of the child could be felt freely movable above the pelvic brim. A quarter of an hour later a large blood clot was expelled, followed by free hemorrhage. Version was at once performed, but the patient suffered severe shock. Extraction of the child was followed by the discharge of a very large quantity of dark blood and the placenta had partially separated. It was at once removed, the uterus douched and packed with gauze. The patient's condition was desperate, but she rallied under stimulation. There was at first no sugar found in the urine immediately after labor. When the gauze was removed from the uterus, streptococci were found upon microscopic examination. Antistreptococcus serum was injected and sugar appeared in considerable quantity in the urine. The patient became actively delirious and abundant acetone appeared in the urine. The temperature fell; the patient shortly afterward died in coma. Upon autopsy the cortex of the kidneys was found in fatty degeneration, there was ulcer of the stomach, arteriosclerosis of the aorta, and hyperæmia and œdema of the lungs. There was dissecting metritis.

This case presented polyhydramnios and diabetes as coexisting conditions. The immediately complicating circumstance which led to the patient's death was severe hemorrhage. Upon examining the uterus, the connective tissue was found necrotic, while the muscle fibre was intact. The lamellated structure of the uterine muscle could still be discerned, although the nuclei could not be seen. Abundant bacteria were present in the vessels.

Leukocytosis in the Complications of Pregnancy and the Puerperal State.—CARMICHAEL, in a recent paper before the Edinburgh Obstetrical Society (*British Medical Journal*, December 5, 1903), found that leukocytosis was an unsafe guide as a symptom unless taken in connection with other well-defined conditions. In some severe cases of puerperal septic infection there was no leukocytosis. In eclampsia an increase in leukocytosis often accompanied a diminution in the severity

of the attacks. No leukocyte count was of much value in determining the necessity for puerperal hysterectomy.

A Clinical Comparison of Pelvis and Fœtus.—LANE (*Lancet*, September 26, 1903) has made a clinical study of the development of Indian children and of the size of the pelvis in the mother.

In measuring the pelvis, advantage was taken of the relaxed condition of the abdominal walls after labor, and the conjugate was measured by pressing the tip of the middle finger strongly against the promontory of the sacrum and depressing the end until its radial edge came in contact with the anterior edge of the symphysis. This manipulation is successful when the uterus has undergone sufficient involution to descend into the pelvic cavity. It was observed that when the dark and white races mixed the result seemed to be the lessening in the pelvic diameters of the white individual. The average conjugate diameter among Indian natives was 4.008 inches, the average measurement between the spines 7.818 inches, and the average measurement between the crests 9.607 inches. In European women the average conjugate measurement was 4.411 inches, the interspinous diameter 8.24 inches, and the intercristal 10.367 inches. In Indian women the average proportion of the interspinous to the intercristal was 81.828 per cent. In European women this percentage was 79.477.

It was found that there existed a distinct ratio between the size of the child and the conjugate diameter. As the weight of the child increased so did the size of the conjugate diameter. The writer believes that in most cases the moulding of the head is largely due to the soft parts. When the head fits tightly in the pelvic brim it may be compressed by the pelvis during labor and subsequently expanded during its passage through the remainder of the birth canal. He concludes that except in the case of small pelves, a parallelism of the biparietal diameter of the head and the conjugate diameter of the pelvis is the result of natural growth and not of pressure. His conclusions are summed up in the statement that the child grows in utero in such a manner that its size is proportional to that of the mother's pelvis.

OTOLOGY.

UNDER THE CHARGE OF

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On Lumbar Puncture in Endocranial Complications of Otitis.—CHAVASSE and MAHU (*Annales du maladies de l'oreille, du larynx*, etc., pp. 384–479) state that lumbar puncture was introduced in December, 1890, by Quincke, of Kiel, who first employed it with a therapeutic

aim to lower the abnormal pressure in the cerebral ventricles, but afterward as a means to diagnose, recognize, and measure the elevation of this pressure in certain pathological cases. It soon passed into the domain of general medicine and there was not much delay in acknowledging it as an efficacious proceeding of direct investigation of the central nervous system. It is supposed that even as the effusion in the pleural cavity reflects quite exactly the state of the serous membrane which contains it, so the composition of the cerebrospinal fluid undergoes special modification produced by the alterations of the meninges or perhaps of the nervous system itself. It is then, especially in this direction, that researches have been directed, for it is well known that the therapeutic value of lumbar puncture is limited. Empirically in the beginning, lumbar puncture has become a scientific means of exploration. Abroad, especially in Germany, where puncture is done commonly through manometric pressure, the clinical and bacteriological characteristics and the therapeutic value of the cerebrospinal fluid has been studied. In France the study of the cells in the cerebrospinal fluid by Widal, Ravant and Sicard has given a new impetus to this means of diagnosis.

Subject is divided into the following chapters:

I. Technique of Lumbar Puncture, Accidents and Dangers.
II. Technique of the Examination of the Cerebrospinal Fluid.
III. Diagnostic Value of Lumbar Puncture.
IV. Therapeutic Value of Lumbar Puncture.

Chapter I. Under the Technique of Lumbar Puncture, Accidents and Dangers, the anatomy of the lumbar region is first reviewed. In the adult, puncture between the fourth and fifth lumbar vertebræ, that is, in the fourth interlaminar space. In the child, puncture in the third or even in the second space. (Quincke.) In certain cases and especially in elderly people, where the cartilages have ossified, if nothing is obtained in the fourth interspace, repeat it in the third space. The needle is very simple, hollow with short head, made of platinum-iridium, and of sufficient resistance to penetrate without bending or breaking. Outside diameter of $1\frac{1}{2}$ mm., inner diameter of $\frac{8}{10}$ mm. to 1 mm., and a length of 10 cm. for adults; 4 to 5 cm. is sufficient length for infants. The end of the needle should have a shoulder to which a short rubber tube can be fastened to regulate the flow of the liquid. Quincke uses a trocar to which a V-manometer tube filled with water is fastened to measure the pressure. A piece of silver or platinum wire to keep the needle open. Strict asepsis of the instrument and the region to be punctured; also, the hands of the operator. In the faint-hearted an injection of cocaine or a jet of ethyl-chloride may be necessary. The penetration of the deep tissues is almost painless. The position of the patient varied, according to the method of the operator. Some place the patient near the edge of the bed, the back strongly bent, head between the hands, elbows touching the thighs. This is a good position for the operator, but cannot always be taken by the patient, and then again the position causes increased intraspinal pressure which may cause the fluid to flow too rapidly. The patient may take a lateral, or a slightly lateroventral position on the right or left side, the head slightly raised by a pillow. Pressure on the abdomen prevents unseasonable movements on the part of the patient, especially when the needle is suddenly thrust in. In frightened patients and especially those with

meningitis, several assistants may be necessary to get sufficient immobility. This is not easily accomplished in the lateral position.

The point of puncture in the fourth interlaminar space is carried out according to Jacoby's line described in 1895. The liquid falls drop by drop and is best gathered in a sterile centrifugal tube. The needle is withdrawn quickly and the wound stopped by a drop of antiseptic collodion or by a light application of tincture of iodine. There is practically no danger in doing lumbar puncture. Of the difficulties, a dry tap is rarely made. The needle may be too short; strike the vertebræ, or the needle may plug up, or there may be a gelatinous exudate. Again there may be abnormal position of the interspaces, deformity or ossification of the ligaments.

Among the possible accidents, the needle may break, bleeding from a rachidian vein, and, in infants, the aorta could be punctured. It is also possible to injure the filaments of the chorda and cause spasmodic movements of the thighs; these passed away in twenty-four hours. If the fluid is collected too rapidly it may cause pain in the head, vertigo, tinnitus, and irregularity of the pulse. If this occurs, stop the flow and lower the head. Never let the pressure fall below 40 mm. After lumbar puncture there may be nausea or vomiting; a tendency to faint if the flow is too rapid or pressure falls below 40 mm. Often there is headache next day; sleep is impossible. These symptoms increase to the third day and then lessen till the sixth or seventh day.

Death may result, especially in cerebral tumor or uræmia. Cases of death have occurred after aspiration and after chloroform. Death nearly always results by paralysis of respiration. The respiration is first intermittent (Cheyne-Stokes) and then stops. Artificial respiration is of no benefit.

Accidents may be avoided by—

1. Puncture without aspiration even without a Pravaz syringe.
2. Place the patient in a prone position.
3. Never give ether or chloroform.
4. Avoid gathering the fluid too fast or too much.
5. Do not drain off more than 20 c.c. of fluid.
6. Avoid puncture in cases of cerebral tumor and be prudent in uræmic cases.

Chapter II. Technique of the Examination of the Cerebrospinal Fluid. It is important to know—

1. The pressure under which the fluid escapes.
2. Its color diagnosis.
3. The bacteriological investigation.
4. The cytological diagnosis.
5. Its chemical characteristics and its "cryoscopie."

In its normal state the cerebrospinal fluid is clear, transparent, and of a density varying from 1003 to 1004. Its quantity varies from 60 to 150 grams, but can be 300 grams and even 400 grams in old people. In pathological states its color is often altered and its density varies from 1002 to 1009

I. *Pressure.* About 125 mm. of water. In tubercular meningitis and tumors of the brain, 80 to 600 mm.

II. *Color.* Compare a tube filled with sterilized water of the same size as the tube in which the fluid is collected.

III. *Bacteriological Examination.*

1. *Direct examination the quickest:* Inoculation can only be performed in chronic cases and in tubercular meningitis. Among the bacteria found are staphylococci, streptococci, pneumococci of Fraenkel and Weichselbaum, meningococci of Weichselbaum, bacillus of Eberth, bacterium coli, streptococcus of Bonome, bacillus of Koch, etc.

2. *Transplantation and cultures:* Colonies only appear at about the end of fifteen days to three weeks, so that this method is inapplicable. A positive result is of extreme value; a negative result is of no use whatever.

3. *Inoculation of animals:* This method takes at least three weeks.

IV. *Cell Diagnosis.* Normal cerebrospinal fluid contains one or two lymphocytes in each field. If the meninges are irritated or inflamed the elements vary according to the intensity and nature of the process; a qualitative and quantitative reaction at the same time. Three or four cubic centimetres of fluid should be collected, best in a centrifugal tube and placed in the centrifuge ten minutes.

The cells contained in diseased states of cerebrospinal fluid are:

1. Mononuclear lymphocytes with small round nuclei. If they are increased in number or predominate, we call it lymphocytosis.

2. Polymorphonuclear leukocytes.

3. Large mononuclear lymphocytes, which are impossible or very difficult to differentiate in this liquid from the single endothelial cells.

1. Lymphocytosis of the cerebrospinal fluid only signifies the existence of an irritation of the meninges and does not give us any indication of the irritative process. They are observed especially in chronic meningitis (tabes, syphilis) and in tubercular meningitis.

2. The presence of polymorphonuclear leukocytes indicates a severe and acute irritation. Observed in acute meningitis, non-tubercular form, with pneumococcus, staphylococcus, and meningococcus, etc. In the first days of the disease the polynuclear leukocytes are very numerous and diminish as convalescence is established; the lymphocytes take their place and, having predominated, disappear as recovery takes place.

3. The cerebrospinal fluid remains normal when there is no anatomical lesion of the meninges. This is the case in cerebral tumor, hysteria, "meningisme" neurasthenia, thrombophlebitis of the sinus, cerebral abscess without complications, etc. The leukocytic formula of a meningitic exudate is in relation to the anatomical reaction which has caused it.

V. *Chemical Properties.* These researches have not been of much practical value.

VI. *Cryoscopy and Hæmatology.* Normally the point of coagulation of serum is about 0.56. That of cerebrospinal fluid is lower; it varies between 0.72 and 0.78. In diseased conditions it varies between 0.56 and 0.74, and in the large majority of cases between 0.60 and 0.65. The hæmatology is of less value than the point of coagulation. The results have little practical bearing as yet.

Chapter III. The Diagnostic Value of Lumbar Puncture. Diagnosis of the endocranial complications of otitis, especially in the early stage, when a judicious intervention could save the life of the patient, often presents great difficulties, sometimes even insurmountable. It is often necessary to ask, in cases with cerebral phenomena well accentuated

but poorly defined, whether a true complication exists, and what, a sinus thrombophlebitis, abscess, meningitis especially in children, or an affection with localized meningitis, cerebrospinal meningitis, tubercular meningitis, or whether a simple reflex phenomenon. Is it "meningisme" hysteria or neurasthenia? The importance of deciding what to do in these difficult cases is such that the specialist is under obligations to try all means of exploration which general medicine provides to solve these hard problems. It is not indifferent in effect to go on an error of diagnosis, open the skull, explore the meninges, and puncture the brain to find an abscess which does not exist, or inversely to do nothing, believing a diffuse bacterial meningitis or tuberculosis when a thrombophlebitis or a brain abscess exists.

Lumbar puncture which permits the examination of the fluid in direct contact with the meninges, the brain, and the spinal cord, gives us knowledge of the actual state, the means of establishing with certainty the presence of an otitic complication, or of revealing the existence of an intercurrent meningeal affection. The study of these questions is the object of this chapter, which is the most important of our report.

I. *Thrombophlebitis of the Sinus, Particularly of the Lateral Sinus.* The cerebrospinal fluid is of normal composition, but its quantity, according to the Halle Clinic, shows an important increase. This fact has not been verified by French observers in cases of thrombosis without complications.

II. *Abscess of the Cerebrum and Cerebellum.* When the abscess is not complicated by other endocranial affection, sinus thrombophlebitis, diffuse or circumscribed meningitis, the liquid is as a rule normal, clear, without micro-organisms, and does not coagulate.

III. *Bacterial Meningitis.* Sicard has divided bacterial meningitis into three groups:

1. Bacterial meningitis caused by pneumococcus, staphylococcus, streptococcus, bacillum of Eberth, colon bacillus, bacillus of Pfeiffer, bacillus pyocyaneus and tetragenus.

2. Epidermic cerebrospinal meningitis due to the meningococcus of Weichselbaum.

3. Serous meningitis which represents the first stage of meningeal infection, the inflammatory exudate remaining serous without terminating in pus, and in which one finds pneumococcus, staphylococcus, bacillus of Pfeiffer and of Eberth, that is, nearly all the bacilli of the first group. Among the meningeal inflammations diffuse suppurative meningitis, caused by bacteria of different kinds, is most frequently observed as a complication of suppurative otitis.

Diffuse Suppurative Leptomeningitis. The suppuration in the majority of cases is in the meshes of the subarachnoid space, exceptionally in the subdural space. Thus, as a rule, suppurative meningitis occurs as a sole complication of an aural affection or accompanies at the same time a sinus thrombosis or a brain abscess. The cerebrospinal fluid obtained by lumbar puncture shows changes in its composition. It shows a varying disturbance, from greenish-yellow to true purulence, and contains a marked quantity, or predominating quantity, of polynuclear leukocytes and very often micro-organisms of different kinds. The pressure under which it is collected is variable, on an average somewhat increased. The predominance of polynuclear

leukocytes here plays an important part and indicates the existence of a meningitis or a meningeal irritation. There are exceptions to this rule where the brain has been found covered with pus and the cerebrospinal fluid clear, normal, or without polynuclear leukocytes.

IV. *Circumscribed Suppurative Meningitis.* Here we may have the same symptoms as in a diffuse meningitis. The puncture is not always demonstrative and can show a normal fluid. In all negative lumbar punctures in the course of symptoms of otitic meningitis there is the possibility of a circumscribed meningitis.

V. *Extradural Suppuration; Internal Suppurative Pachymeningitis; Intradural Abscess.* In these suppurative inflammations the cerebrospinal fluid is normal in composition

VI. *Serous Meningitis.* Serous meningitis is still poorly defined. We find described under this class bacterial meningitis not yet come to suppuration; meningitis from absorption of toxins, from suppurative ears, the temporal bone or the brain. Then the serous meningitis of Quincke. Serous meningitis is observed almost exclusively in infancy or youth and sometimes shows true meningeal symptoms; it takes most frequently a subacute course with tendency to dropsy of the ventricles, giving rise to symptoms of cerebral pressure, clinically like a cerebral abscess, with which it is frequently confused.

Merkens, Brieger and Körner believe that the great majority of cases of serous meningitis are due to the absorption of toxins from a suppurative seat producing a serotoxic inflammation of the meninges leading to an internal hydrocephalus. A sufficient number of observations of the cerebrospinal fluid has not been made to draw conclusions, though it is generally clear and under pressure.

VII. *Cerebrospinal Meningitis.* Due to the meningococcus of Weichselbaum. The cerebrospinal fluid is generally of a greenish tint and slightly cloudy. It can be purulent. Councilman has found it mostly clear. Dr. Councilman observed the diplococcus of Weichselbaum thirty-eight times in fifty-five cases.

VIII. *Tuberculous Meningitis.* Most common in infants, caused by an otitic, or concomitant with, a general tuberculosis. Rarely it has been confounded with an ordinary meningitis or even with a brain abscess. The fluid obtained by puncture is most often clear, limpid, sometimes greenish-yellow, or tinted with blood. It is collected generally under increased pressure. The coagulum which forms is white, dull or gray, hard. The bacillus of Koch is found in about 50 per cent. of cases and always in small numbers. The lymphocytes predominate. The accuracy of information derived by lumbar puncture has put aside all ideas of intervention.

IX. *"Meningisme." Pseudomeningitis of Bouchut.* A simulation more or less perfect of meningitis by a process independent of all cortico-meningeal lesions. Cases where no inflammatory lesion can be suspected. It should be distinctly separated from serous meningitis. Sometimes observed in suppurative otitis and to be diagnosed from simple or tubercular meningitis or cerebral abscess. Occurs in youth and also in the adult. Attributed to hysterical neurasthenic meningitis, non-bacterial intoxication, or toxins from pneumococcus, or reflex symptoms from suppurative labyrinthitis.

X. *"Labyrinthisme."*

XI. *Traumatic Lesions of the Labyrinth and of the Base of the Skull.* Two cases cited by Moure. Numerous blood globules in the cerebrospinal fluid.

XII. *Influences Exercised by Certain Diseases on the Cerebrospinal Fluid.* 1. Syphilis. 2. General paralysis. Tabes. 3. Chronic alcoholic meningitis. 4. Mental aberration, senile dementia. 5. Hysteria and neurasthenia.

Discussion on the Diagnostic Value of Lumbar Puncture. The following conclusions are generally true, but not constant:

1. Clear liquid, normal, non-coagulable; thrombophlebitis of the sinus, brain abscess supra and subdural, serous meningitis so-called simple; "meningisme," hysteria, sometimes circumscribed meningitis. If the fluid gathers in a stream under pressure, very great probability of a sinus thrombophlebitis, serous meningitis or sometimes abscess of the brain.

2. Clear liquid, without bacteria or cells forming a coagulum; meningitis probable, perhaps by toxins (?), sometimes tuberculous.

3. Clear liquid or yellowish or slightly cloudy with lymphocytosis predominating, or the bacillus of Koch: tubercular meningitis (eliminate clinically the causes of lymphocytosis if the bacillus of Koch is not found).

4. Fluid opalescent or purulent, forming coagulum with polynuclear leukocytes predominating, and eventually micro-organisms of different kinds; acute suppurative diffuse meningitis or non-suppurative cerebrospinal meningitis if there is the meningococcus of Weichselbaum and if the puncture is early, sometimes circumscribed meningitis. This is quite exceptional in brain abscess.

Then for differential diagnosis of the different kinds of meningitis and meningitis and brain abscess, simple serous meningitis, "meningisme" and sinus thrombophlebitis, lumbar puncture with its color, bacterial and cell diagnosis of the cerebrospinal fluid, does not give us an absolute diagnosis but one of great importance, especially if we are aided by clinical observation.

Chapter IV. Therapeutic Value of Lumbar Puncture. In practical otology, in meningeal complications, lumbar puncture seems as if it could be therapeutically of a certain utility, at least as a means to suppress the initial seat of suppuration. If one decides to use it for this effect one must, following the advice of Netter and Sicard, withdraw each time 20 to 30 c.c. of fluid and repeat the lumbar puncture as many times as one deems it necessary.

Conclusions. 1. Lumbar puncture is a valuable means of diagnosis in intracranial complications of aural suppuration on condition that an examination of the cerebrospinal fluid is made as to its color, bacteriology, and cytology. Lumbar puncture without aspiration, without general anæsthesia, and with the patient lying down is almost always without danger.

2. Positive as well as negative results should be considered, also the clinical status and the exact stage in which the puncture is made. The influence of certain general diseases on the condition of the cerebrospinal fluid must not be overlooked.

3. The existence of a bacterial meningitis is indicated in the great majority of cases, if the liquid is turbid or even clear after centrifugalization and contains bacteria or polynuclear leukocytes or both. A clear

liquid or one slightly turbid, containing mononuclear lymphocytes in abundance, indicates as a rule tubercular meningitis, positively, if it contains the bacillus of Koch. Lymphocytosis is also seen in other chronic meningeal affections and in the convalescence from acute meningitis, especially in cerebrospinal meningitis.

4. In extradural and subdural suppuration the cerebrospinal fluid remains normal so long as the arachnoid membrane is free from all irritation.

5. Lumbar puncture in circumscribed meningitis up to the present has not given much satisfaction as an aid to diagnosis of these affections.

6. In brain abscess, in thrombophlebitis of the lateral sinus, and in the serous non-bacterial meningitis the fluid is clear and normal, often increased in quantity and under increased tension, more in the last two complications.

7. The fluid is normal in "labyrinthisme" and "meningisme."

8. After traumatic lesions of the labyrinth or base of the skull with ear symptoms, red blood corpuscles are often found in the cerebrospinal fluid.

9. The condition found in the fluid should never stop surgical intervention; on the contrary, the operator should be more exact in his purpose, starting effectively.

10. Till now the therapeutic value of lumbar puncture has been doubtful; nevertheless, considering the results obtained in general medicine and in some cases of meningitis of otitic origin, lumbar puncture may be performed, together with surgical intervention, so long as the situation does not appear hopeless clinically.

11. Lumbar puncture has demonstrated curability of certain cases of meningitis.

12. Examination of the cerebrospinal fluid, particularly as to its cellular characteristics, makes a great step forward in the diagnosis of intracranial complications of otitis, and we think it ought to be generally employed.

DERMATOLOGY.

UNDER THE CHARGE OF

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A Tuberous Iodide of Potash Eruption Simulating, Histologically, Epithelioma.—D. W. MONTGOMERY (*Journal of Cutaneous Diseases*, February, 1904) reports the following case: A man, aged fifty-two years, who, fifteen years previously had had a sore upon the penis followed by a generalized scaly eruption, presented an eruption of tumor-like and papillary elevations scattered over the scalp, face, trunk, and

extremities after taking considerable doses of iodide of potassium. The eruption was accompanied by some elevation of temperature and evidences of renal insufficiency. One of the most characteristic lesions, situated on the forehead over the left eye, was a quarter-dollar-sized, soft, rounded tumor with a broad, constricted base and ulcerating summit. A portion of this tumor examined microscopically showed a structure closely resembling epithelioma, there being the same connective-tissue *loculi* filled with atypical epithelial cells. The author calls attention to the ease with which mistakes in the microscopic diagnosis of such lesions may be made.

Sublamine in Parasitic Diseases of the Scalp.—W. S. GOTTHEIL (*Medical News*, October 17, 1903) found this drug valuable in an epidemic of tinea tonsurans in New York, where out of 900 children in an orphan asylum, 450 were affected. A solution of 1:1000 proved less irritating than corrosive sublimate and was found to cause less inflammatory reaction, and cures were quicker with the new remedy than with the old. The author states that a fungus not to be distinguished from the trichophyton could be cultivated from the scalps of persons who seemed to have no disease.

The Varieties of Lineæ Albicantes.—W. OSLER (*Medical News*, November 7, 1903) divides lesions of the kind into three groups: first, those due to distention of the skin, as observed in ascites and pregnancy; secondly, post-febrile instances, especially such cases as are met with after scarlet and typhoid fever; and thirdly, the idiopathic form. The author gives the notes of a case of an adult in whom after typhoid fever transverse scar-like lines developed in the sacral region. Some cases are difficult of explanation.

Periodical Shedding of the Hair.—H. LEDERMANN (*Journal of Cutaneous Diseases*, January, 1904, p. 53) describes the case of a woman, aged twenty-two years, whose hair was shed every winter and grew in again in the summer. Last winter she became entirely bald, and this summer her hair did not grow in again. Absence of hair existed on the general surface, which began in circular patches when she was twelve years old.

A Case of Systemic Blastomycosis, with Multiple Cutaneous and Subcutaneous Lesions.—ORMSBY and MILLER (*Journal of Cutaneous Diseases*, March, 1903) report a case of systemic blastomycosis—the third on record—accompanied by numerous cutaneous lesions. The patient, a Swede, fifty-six years old, ten years before his death exhibited symptoms of pulmonary disease accompanied by fever, weakness, and emaciation. Two months after the beginning of this illness cutaneous lesions appeared which consisted of cutaneous and subcutaneous nodules and abscesses, and open and crusted ulcers extensively distributed over the entire body, but most abundant upon the head, face, and extremities. Pure cultures of blastomycetes were obtained from the abscesses ante-mortem and from various tissues and organs post-mortem. Microscopic examination of the various lesions failed to show any tubercle bacilli, but revealed great numbers of blastomycetes. No reaction to tuberculin was obtained, and experiments upon animals

were likewise negative as to tuberculosis. At the autopsy the lungs were found to contain great numbers of abscesses and tubercle-like lesions; the pleura was studded with nodules, and the liver and kidneys contained many miliary abscesses and nodules. The spleen was extensively diseased, portions of it being practically destroyed. The mesentery contained many nodules. Blastomycetes were demonstrated microscopically and culturally in all these situations, but no tubercle bacilli. While the early pulmonary and other symptoms and the patient's family history suggested tuberculosis, the failure to demonstrate the tubercle bacillus by any of the methods employed for this purpose, the absence of the histological features characteristic of tubercular tissue, the extraordinary number and rapid evolution of the cutaneous lesions, and the great numbers of blastomycetes in every lesion, in the opinion of the authors, exclude tuberculosis.

Pemphigus Neonatorum in the Light of Recent Research.—H. G. ADAMSON (*ibid.*) concludes from his investigations that it is generally admitted that pemphigus of the newborn is an infantile form of impetigo contagiosa, and that it is due to streptococcic infection. It would seem therefore reasonable to suppose that observers who have described the staphylococcus pyogenes aureus as the infective agent in pemphigus of the newborn have been concerned with a secondary infection, and that investigation by special culture methods will discover the streptococcus pyogenes as the primary cause.

Tinea Versicolor of the Finger Nails.—CAMPANA, of Rome (*Journal of Cutaneous Diseases*, January, 1904), cites a case in which the fingers and finger nails were affected. For a long time prior to the appearance of the disease on the fingers the nails had been thickened. The microscope showed the presence of the mycelian and sporon of the microsporon furfur.

Pityriasis Rosea.—WEISS (*Journal of the American Medical Association*, July 4, 1903), in a paper read at the Fifty-fourth Annual Session of the American Medical Association in the Section on Cutaneous Medicine and Surgery, reports the results of his study of this affection. He believes the disease to be of internal origin, due to some pathogenic substance circulating in the blood. Microscopic examination of scales and sections and culture experiments failed to reveal any fungus in the cases which he has studied. The microscopic picture presented by the malady is that of a mild subacute exudative inflammation affecting the cutis chiefly.

Acute Contagious Pemphigus in the Newly Born.—G. J. MAGUIRE, of London (*British Journal of Dermatology*, December, 1903), presents an interesting paper on a subject about which there is not much definite knowledge. A series of 18 cases is given, illustrating an epidemic of this disease. The author summarizes his experience as follows: That his cases, occurring epidemically, belonged to the group designated pemphigus acutus neonatorum. The disease was due to a pathogenic micro-organism, the staphylococcus pyogenes aureus, conveyed from case to case by a certain midwife. While occurring chiefly in the newly born, and only fatal to these, it also attacked older children and adults.

It was characterized by a bullous eruption on the skin, variable in distribution and extent, the specific organism being found in the contents of the blebs. In many of the cases no symptoms other than the skin eruption were manifested, but a certain group of cases showed grave symptoms of a general infection, and invariably ended fatally. The point at which the systemic invasion arose in these fatal cases was the unhealed umbilical scar. The treatment had little or no effect upon the course and duration of the disease, whatever the result.

Influence of the Becquerel Rays upon the Skin.—HALKIN (*Archiv für Dermatologie und Syphilis*, Bd. lxv., Heft 2), experimenting with radium-barium bromide upon the skin of young pigs, found that effects very similar to those produced by the Roentgen ray were produced. After exposures of varying length, the portions of skin exposed were excised and examined microscopically. It was found that the Becquerel rays acted upon the vessels, the epithelium, and the connective-tissue cells much in the same way as the Roentgen rays. Experiments were then made to determine whether these rays might be employed therapeutically, lupus vulgaris being the disease selected for the experiments. Exposures of moderate duration were apparently without effect. After exposures lasting from two to four hours, repeated daily for from fourteen to nineteen days, ulceration followed; but even in these cases the most careful microscopic examination failed to show any effect upon the deeper portions of the lupus deposit.

Six Cases of the Miliary Perifollicular Syphiloderm Resembling Lichen Scrofulosorum and Lichen Pilaris.—JONITESCU (*Annales de Derm. et de Syph.*, June, 1903) describes the pathological anatomy of five cases which consisted of a perifollicular cellular deposit of plasma cells, with here and there giant cells, such as are commonly met with in the papular syphilodermata, the peculiarity being that they were perifollicular.

A Case of Chronic Purpuric Erythema (Eight Years' Duration), with Pigmentation of Skin and Enlargement of Liver and Spleen.—OSLER (*Journal of Cutaneous Diseases*, July, 1903) reports the following unusual and interesting case: A man thirty-three years old was admitted to the Johns Hopkins Hospital, complaining of an extensive cutaneous eruption and soreness of the wrists, ankles, and knees. The illness had begun seven years before with red spots about the ankles, and from that time the legs had never been free from eruption, which gradually grew worse, spreading slowly up the legs. Some years later spots appeared upon the arms. The face remained free. The eruption was not accompanied by itching. For a year past there was a good deal of pain in the joints, chiefly pain on motion, but no swelling nor redness. When admitted to the hospital the legs presented an almost uniform, deep brownish pigmentation with here and there lighter areas; widespread areas of hemorrhagic infiltration into the skin; localized and distinctly raised areas of hyperæmia and hemorrhage resembling purpura urticans, and lastly a general scaliness. The condition extended to the groins in front and to the sacral region behind. The skin was hard and brawny to the touch. The greater part of the back was free, but there were a few spots above the sacral region and in the left inter-

scapular area. Upon the left arm along the posterior axillary fold were linear ecchymoses, and a few spots of hemorrhage and infiltration over the biceps. The spleen and liver were both enlarged. The patient improved decidedly during his stay in the hospital. The continuous warm bath was used, the patient remaining seventeen or eighteen hours in the tub. The skin improved very much, but fresh hemorrhages occurred at intervals. Examination of the skin excised from the leg showed much iron-containing pigment in the connective tissue of the corium, and an increase in the small mononuclear elements. Six months later the condition of the skin had changed very little. About one year after the last examination the patient died of pernicious malaria.

PATHOLOGY AND BACTERIOLOGY.

UNDER THE CHARGE OF

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Report of Investigation of Spotted Fever.—WILSON and CHOWNING (*First Biennial Report of the Montana State Board of Health*). The disease known in Montana as "spotted fever" has been recognized as a distinct clinical entity by physicians of the Bitter Root Valley for fifteen to twenty years. It is confined to the eastern foot-hills of the Bitter Root Mountains in a valley on the western side of the Bitter Root River, but outside of this comparatively small area the disease is rarely if ever seen. Spotted fever is met with only in the spring months, appearing between March and July. Persons who are constantly out-of-doors upon the foot-hills and mountains are the ones oftenest attacked, and apparently for this reason the disease is more common in males than in females. The mortality is very high; 70 per cent. to 80 per cent. of the cases end fatally. Death usually occurs between the sixth and eleventh days of the disease, but should the termination be favorable the attack is prolonged, and convalescence is slow. An initial chill usually marks the onset of the disease, while the early symptoms are headache, backache and joint pains. The general appearance is much like that of typhoid fever. After the initial chill the temperature rises to 103° or 104° F., and in five to seven days may reach 105° or 107° F. If the patient recovers the temperature usually falls by lysis. The eruption, which has given the name to the disease, makes its appearance from the second to the fifth day after the chill, spreading from the wrists, ankles and back over the entire body. At first the rash is macular, of a rose-red hue, and disappears on pressure; but later the spots become permanent, much larger, and assume a deep purple hue. Purplish

petechiæ may be present. The skin ordinarily shows some jaundice, and the vessels of the conjunctivæ are injected. Superficial gangrene, pneumonia, and articular rheumatism may arise as complications. At autopsy no specific lesions are found. All the organs are congested and show the evidences of an acute infection.

In the red blood cells of the circulating blood the authors found an organism which they believe is a hitherto undescribed hæmatozoon. In a fresh drop of blood from the patient's ear the parasites are not very numerous, though they may be found with careful search during the entire course of the disease. As far as may be determined, two stages can be recognized in the life-cycle of this parasite. In the first phase the organisms appear as small hyaline oval bodies, 1 micron in thickness by 1½ microns in length. Two of these bodies may occur in the same corpuscle. Motility has not been observed. In the second stage oval or irregular solitary bodies are seen within the red blood corpuscles. This form measures from 2 to 3 microns in breadth and 5 microns in length; it is actively amœboid, and constantly throws out and draws in small pseudopodia, thus changing its shape with great rapidity. The parasites are readily stained by methylene blue, Nocht-Romanowsky, hæmatoxylin and Jenner's mixture. While the organisms are scarce in the circulating blood, they may be found in abundance within the red blood cells of the internal organs. In sections and smears from the heart muscle, spleen, liver, and kidneys great numbers of red blood corpuscles are seen containing parasites, and frequently many phagocytes are observed which have absorbed one to eight infected red blood cells.

By means of subcutaneous inoculations of spleen and heart's blood from autopsy cases the disease can be transmitted in a mild form to rabbits, and for many days the red blood corpuscles of these animals are found to harbor parasites. The mode of infection is believed to be through tick bites, although direct proof of this means of transference is not yet established. The tick is not suspected, however, of carrying the parasite from man to man, but is considered to act as an intermediate host and to receive the parasite from the "gray gopher" or "ground squirrel." This rodent is plentiful in the infected district, and, moreover, its geographical and seasonal distribution bears a close relationship to the situation and occurrence of "spotted fever." Several "gray gophers" were captured, and in the blood of many of these animals parasites were found which were similar in all respects to those seen in the red blood corpuscles of the blood from cases of spotted fever.

The interesting fact was also noted that only the gophers from the west side of the river harbored parasites, while those from the east side, where spotted fever does not occur, were entirely free from the infection. The authors in concluding suggest that many points will have to be investigated before the study of the disease or its mode of transmission can be completed.

On a Dysentery Antitoxin.—CHARLES TODD (*Brit. Med. Jour.*, 1903, vol. ii. p. 1457) concludes from his work upon dysentery antitoxins that by growing the dysentery bacillus in a somewhat highly alkaline broth a soluble toxin is obtained. Certain animals, notably the horse and rabbit, are highly susceptible to this toxin. The toxin is fairly stable, and though destroyed by an exposure to a temperature of 80° C.

for an hour, it is not altered by exposure to a temperature of 70° C. for the same period. When injected into suitable animals, for example the horse, the toxin gives rise to a powerful antitoxin. The combination of the toxin and antitoxin "in vitro" does not take place immediately, but requires a certain time, and the rate of combination varies with the temperature.

Bacteriological and Anatomical Studies of Scarlet Fever, with Special Reference to Blood Examinations.—JOCHMANN (*Deut. Arch. f. klin. Med.*, Bd. lxxviii. p. 209) contributes an interesting article upon this subject. In 161 cases of scarlet fever streptococci were found in the blood twenty-five times during life, pneumococci twice, and paratyphoid bacilli once. Streptococci were never isolated from the blood during the first two days of the disease, nor from the blood of any of the fulminating cases. Their presence was always coincident with some secondary infection, usually a tonsillitis. All the cases from which positive cultures were obtained ended fatally, death occurring within one or two days. The bacteriological examination of 70 autopsy cases showed that in a very large proportion streptococci were present not only in the heart's blood, but in the spleen, bone-marrow, and less frequently in the kidney. This streptococcic infection appeared as a secondary event in the course of the disease. The usual portal of entry was the tonsils. In all but one of the cases showing streptococci in the blood during life, microscopic examinations of the tonsils after death revealed very definite lesions with accumulations of streptococci in the bloodvessels and lymphatics of the surrounding tissues. The one exception was a case of otitis media with mastoid infection. The author concludes that streptococcic infection plays an exceedingly important role in scarlet fever, although the condition has no etiological significance and must be considered as a secondary event.

The Pathological Anatomy of Whooping-cough and the Presence of the Whooping-cough Bacillus in the Organs.—ARNHEIM (Virchow's *Archiv*, 1903, Bd. clxxiv. p. 530) concludes, from a study of eight fatal cases of whooping-cough, that the disease is an infectious catarrh of the mucous membrane of the respiratory tract, affecting particularly the trachea. In the secretion of the air-passages and in their mucous membranes it is possible to demonstrate the characteristic polar-staining bacillus, which has been described by Czaplewski as the exciting cause of the affection. The bacilli often occur in colonies. A desquamative catarrh is usually present. Great numbers of bacteria are found in the bronchopneumonic patches in the lungs. The onset of the characteristic coughing spells is caused by the presence of bacterial colonies in the typical "cough areas," the situation of which Nothnagel and Kohts have described. The coughing spells should thus be considered as a healing process, since with the expectorated sputum innumerable bacteria are carried away. The secretion is viscid. Healing follows with *restitutio ad integram* after the expulsion of the colonies of bacteria from the mucous membrane.

Periarteritis Nodosa.—VESZPREMI and JONCSO (*Ziegler's Beit.*, 1903, Bd. xxxiv. p. 1) say this affection was first described by Kussmaul and Maier in 1866, but it is of such rare occurrence that the authors have

only been able to collect eight authentic cases reported since that time. The case under discussion was that of a boy, aged fourteen years, who for six months before death had had occasional choreiform attacks and a petechial eruption over parts of the body. He was admitted to the hospital with symptoms of cerebral hemorrhage. At autopsy a large hemorrhage was found over the cortex of the cerebrum. Multiple miliary aneurisms were discovered in the coronary arteries and in the lesser arteries of the stomach and intestines, besides which there were small nodules situated above the vessels and occasional thromboses, giving rise in the heart to disseminated areas of necrosis. Histological examination of the aneurisms and periarteritic nodules showed that the earliest change consisted in an invasion of the adventitia of the smallest vessels by great numbers of leucocytes, while in a later stage the process extended to the media and produced grave defects in that coat. Owing to these alterations the vessel walls appeared unable to withstand the blood pressure, and therefore the coats were stretched and thinned, or the elastica torn into short fibres. In the more advanced lesions the infiltration of leucocytes had subsided, and connective tissue cells made their way from the adventitia through the media and elastica into the intima, overgrowing and replacing the leucocytes. The hyaline-like band described by Meyer, Graf, Müller, and Freund which lies between the thickened intima and the atrophied media was formed by a coagulation necrosis of the exudate in the vessel walls. The authors conclude, in reviewing the cases so far recorded, that the symptomatology of the disease is so varied and confusing that one can scarcely recognize the affection clinically as an entity. They emphasize particularly the fact that the changes in the vessels and thickening of the intima especially are dependent upon a process which originates in the adventitia of the arteries.

Lesions of the Red Bone-marrow in Typhoid Fever, with Special Reference to the Vertebræ.—E. FRAENKEL (*Mit. aus den Grenzgeb. der Med. u. Chir.*, 1903, Bd. x. p. 1) says that in 1894 Quincke made the announcement that he had found typhoid bacilli in the bone-marrow of eight out of nine cases of typhoid fever. Since then his observations have been confirmed by other authors. Fraenkel investigated thirteen cases of typhoid, and in every instance recovered typhoid bacilli in great numbers from the marrow of the vertebræ. The presence of the bacilli in the bone-marrow bore no relation to their numbers in the blood; in the former situation they were found as late as the sixth week of the disease. Sections from the bone-marrow of the femur and vertebræ showed definite histological lesions. Besides hemorrhages, accumulations of small round cells, and diffuse areas of degeneration, changes which may occur in other varieties of acute infections, and were not considered specific, certain other lesions which the author believes are peculiar to typhoid fever were found with great constancy. These lesions consisted in small areas of focal necrosis infiltrated with a delicate network of fibrin threads, but not surrounded by a zone of reaction. They are probably produced by a slow action of the typhoid toxin upon the bone-marrow cells and upon the lymphatics, in the latter case causing rupture of the wall of the lymph vessel and an escape of lymph, thereby giving rise to the mesh of fibrin lying between and about the necrotic cells. Typhoid bacilli were not necessarily associated with the lesions. The

condition is not known to occur in diphtheria, scarlet fever, erysipelas, pneumonia or peritonitis, but in variola Chiari has described somewhat similar areas. The author believes these areas of focal necrosis are as characteristic of typhoid fever as any of the histological lesions found in the other organs, and suggests the name of "osteomyelitis typhosa" to describe the condition.

The Dysentery Bacillus in a Series of Cases of Infantile Diarrhœa.—WOLLSTEIN (*Journal of Med. Research*, 1903 vol. x. p. 10) during the past winter examined the stools in one hundred and fourteen cases of infantile diarrhœa occurring in New York. In thirty-nine instances she was able to isolate the B. dysenteriæ (Shiga). The clinical picture of dysentery associated with frequent bloody and mucous stools was present in most of the positive cases; but in some stools, though mucus was noted, there was no blood. For early diagnostic purposes the serum reaction could not be relied upon, since it rarely occurred during the first week, and frequently was not positive for two weeks. The isolation of the B. dysenteriæ from the stools was the only positive evidence of infection during life. The bacilli were found in the stools for a period of two to three weeks, and they occasionally remained for a longer time.

A Study of the Proteolytic Enzymes and of the So-called Hæmolysins of Some of the Common Saprophytic Bacteria.—ABBOTT and GILDERSLEEVE (*Journal of Med. Research*, 1903, vol. x. p. 42) conclude from their experiments made with the filtered products of the growths of B. prodigiosus, B. proteus vulgaris, B. subtilis, etc., in gelatin, bouillon, and other media that the destiny of these non-toxic but otherwise physiologically characteristic products of bacterial life in the body is determined by the presence of a specific neutralizing substance that can be demonstrated in the circulating blood. By the customary methods of artificial immunization the amount of such antidotal substances in the blood may be increased, though only to a slight degree; and through the use of sera from animals immunized from the non-toxic bacterial products it is possible to distinguish the proteolytic enzymes resulting from the growth of different bacterial species from one another as well as from certain physiologically analogous enzymes of animal origin such as trypsin.

The proteolytic enzymes elaborated by certain bacteria in the course of their growth are much more resistant to high temperatures than is generally supposed, some being capable of exhibiting their characteristic function after exposure in the moist state to a temperature of 100° C. for fifteen to thirty minutes. The so-called hæmolysins of bacterial origin, are at least in some cases proteolytic enzymes. The authors believe that it is possible by experimental means to contribute material support to the doctrine of Welch concerning the origin of bacteriogenic cytotoxins.

Experimental Researches in the Inoculation of Syphilis in the Monkey ("Bonnet Chinois").—NICOLLE (*Ann. de l'Instit. Past.*, 1903, T. xvii. p. 636) reports three experiments which were made before Metschnikoff's and Roux's communication, but which have hitherto remained unpublished. The cutaneous inoculation of three monkeys with the products of chancre resulted in the development, after fifteen

to nineteen days' incubation, of certain local lesions. Papules appeared at the site of inoculation in two cases and in one case a hard indurated nodule, together with swelling of the adjacent lymph glands. The local lesions soon disappeared and no further symptoms suggestive of syphilis made their appearance.

Protozoa in a Case of Tropical Ulcer (Delhi Sore).—WRIGHT (*Jour. of Med. Research*, 1903, vol. x., p. 472), while studying a case of tropical ulcer, found certain peculiar bodies in both smear preparations and stained sections which he believes are protozoa and the cause of the condition. For the staining of these bodies in smear preparations the best results were obtained by using the methylene-blue-eosin mixture which the author has previously described. The bodies are generally round, sharply defined, and from 2 to 4 micromillimetres in diameter. A large part of the periphery stains a robin's egg blue, while the central portions are unstained or white. A prominent feature is a small lilac-colored mass which always appears near the periphery. The bodies are found in great numbers and often occur within cells. In sections the cortical portion stains faintly with nuclear stains, while the peripheral mass, considered to be the nucleus, stains deeply with methylene blue or gentian violet. It is possible that these same cells have been described before by Cunningham and Firth. All efforts to reproduce the lesions in rabbits by subcutaneous injections of material obtained from the ulcer were attended with negative results. It was also impossible to cultivate the organisms upon fresh human blood or other media. Wright suggests the name of *helcosoma tropicum* for this newly described parasite.

Pale Cells in the Human Liver.—ADLER (*Ziegler's Beit.*, 1903, Bd. xxxv. p. 127) has found that in the liver of the human fœtus two different varieties of liver cells can be distinguished. Besides the ordinary polygonal cells large, rounded, pale cells are seen, which, from their small fat and pigment content and the presence of mitotic figures must be regarded as young liver cells. Between this cell and the ordinary liver cells all grades of transition may be observed. In certain pathological conditions the livers of adults show the presence of pale cells which bear some resemblance to those in the fetal livers. When part of the liver parenchyma has been destroyed and there is a tendency to cell regeneration, as in cirrhosis, red atrophy, primary carcinoma, etc., these pale cells are numerous in the atypical portions of the parenchyma and appear exactly like those in the fetal livers. It is thus possible by histological examination to recognize those portions of the liver where regenerative processes are in progress.

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